# REGENERATION

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BY

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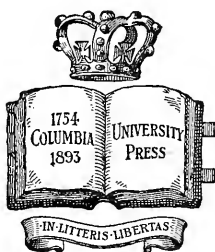
To My Mother

# PREFACE

THIS volume is the outcome of a course of five lectures on "Regeneration and Experimental Embryology," given in Columbia University in January, 1900. The subjects dealt with in the lectures are here more fully treated and are supplemented by the discussion of a number of related topics. During the last few years the problems connected with the regeneration of organisms have interested a large number of biologists, and much new work has been done in this field ; especially in connection with the regenerative phenomena of the egg and early embryo. The development of isolated cells or blastomeres has, for instance, aroused widespread interest. It has become clearer, as new discoveries have been made, that the latter phenomena are only special cases of the general phenomena of regeneration in organisms, so that the results have been treated from this point of view in the present volume.

If it should appear that at times I have gone out of my way to attack the hypothesis of preformed nuclear germs, and also the theory of natural selection as applied to regeneration, I trust that the importance of the questions involved may be an excuse for the criticism.

If I may be pardoned a further word of personal import, I should like to add that it has seemed to me that far more essential than each special question with which the biologist has to deal is his attitude toward the general subject of biology as a science. Never before in the history of biology has this been more important than at the present time, when we so often fail to realize which problems are really scientific and which methods are legitimate for the solution of these problems. The custom of indulging in exaggerated and

unverifiable speculation bids fair to dull our appreciation for hypotheses whose chief value lies in the possibility of their verification; but those who have spent their time and their imagination in such speculations cannot hope for long to hold their own against the slow but certain advance of a scientific spirit of investigation of organic phenomena. The historical questions with which so many problems seem to be connected, and for which there is no rigorous experimental test, are perhaps responsible for the loose way in which many problems in biology are treated, where fancy too often supplies the place of demonstration. If, then, I have tried to use my material in such a way as to turn the evidence against some of the uncritical hypotheses of biology, I trust that the book may have a wider bearing than simply as a treatment of the problems of regeneration.

I wish to acknowledge my many obligations to Professor H. F. Osborn and to Professor E. B. Wilson for friendly criticism and advice; and in connection with the revision of the text I am greatly indebted to Professor J. W. Warren, to Professor W. M. Wheeler, to Professor G. H. Parker, and to Professor Leo Loeb.

Bryn Mawr College, Pennsylvania,
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# REGENERATION

# CHAPTER I

## GENERAL INTRODUCTION

ALTHOUGH a few cases of regeneration were spoken of by Aristotle and by Pliny, the subject first attracted general attention through the remarkable observations and experiments of the Abbé Trembley. His interest was drawn to certain fresh-water polyps, hydras, that were new to him, and in order to find out if the organisms were plants or animals he tried the effect of cutting them into pieces; for it was generally known that pieces of a plant made a new plant, but if an animal were cut into pieces, the pieces died. Trembley found that the polyp, if cut in two, produced two polyps. Logically, he should have concluded that the new form was a plant; but from other observations, as to its method of feeding and of movement, Trembley concluded that the polyp was an animal, and that the property of developing a new organism from a part must belong to animals as well as to plants. "I felt," he says, "strongly that nature is too vast, and too little known, for us to decide without temerity that this or that property is not found in one or another class of organized bodies."

Trembley's first experiments were made in 1740, and the remarkable results were communicated by letter to several other naturalists. It came about in this way that before Trembley's memoir had appeared, in 1744, his results were generally known, and several other observers had repeated his experiments, and extended them to other forms, and had even published an account of their own experiments, recognizing Trembley, however, as the first discoverer. Thus Réaumur described, in 1742, a number of other forms in which regeneration takes place; and Bonnet, in 1745, also described some experiments that he had made during the four preceding years. Widespread interest was aroused by these results, and many different kinds of animals were experimented with to test their power of regeneration. Most important of these new discoveries were those of Spallanzani, who published a short preliminary statement of his results, in 1768, in his *Prodromo*.

B                                                    I

Trembley found that when a hydra is cut in two, the time required for the development of the new individuals is less during warm than during cold weather.   He also found that if a hydra is cut into three or four parts, each part produces a new individual.   If these new hydras are fed until they grow to full size, and are then again cut into pieces, each piece will produce a new polyp.   The new animals were kept in some cases for two years, and behaved in all respects as do ordinary polyps.

Trembley also found that if the anterior, or head-end, with its tentacles, is cut off, it also will make a new animal.   If a hydra is cut lengthwise into two parts, the edges roll in and meet, and in an hour, or less, the characteristic form may be again assumed.   New arms may appear later on the new individual.   If a hydra is split lengthwise into four pieces, each piece will also produce a new polyp.

If the head-end only of a hydra is split in two, each half becomes a new head, and a two-headed hydra results.   If each of the new heads is split again, a four-headed hydra is produced; and if each of the four heads is once more split in two, an eight-headed hydra is formed.   A hydra of this kind, in which seven heads had been produced in this way, is shown in Fig. 1, *A*.   Each head behaves as a separate individual, and all remain united on the same stalk.   If the foot-end of a hydra is split, a form with two feet is produced.

One of the most ingenious and most famous experiments that Trembley made consisted in turning a hydra inside out (Fig. 1, *B*, 1 and 2).   The animal tends to turn itself back again, but by sticking a fine bristle through the body, Trembley thought that the turning back could be prevented, and that the inner surface of the hollow body remained on the outside, and the outer surface of the body came to line the new central cavity.   Each layer then changed, he thought, its original characteristics, and became like that of the other layer.   The details of these experiments will be described in a future chapter, as well as more recent experiments that have put the results in quite a different light.

Réaumur repeated Trembley's experiment of cutting a hydra into pieces, and obtained the same results.   He found also that certain fresh-water worms, as well as the terrestrial earthworm, regenerated when cut into pieces.   At his instigation two other naturalists[1] examined the starfish and some marine polyps, and they concluded that it was highly probable that these forms also could regenerate. Réaumur pointed out that regeneration is more likely to occur in fragile forms which are more exposed to injury.

Bonnet's experiments were made on several kinds of fresh-water

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[1] Guettard and Gérard de Villars.   Bernard de Jussieu also, who demonstrated that starfish can regenerate.

worms, one of which, at least, seems to have been the annelid lumbriculus. His first experiments (1741) showed that when the worm is cut in two pieces, a new tail develops at the posterior end of the anterior piece, and a new head at the anterior end of the posterior
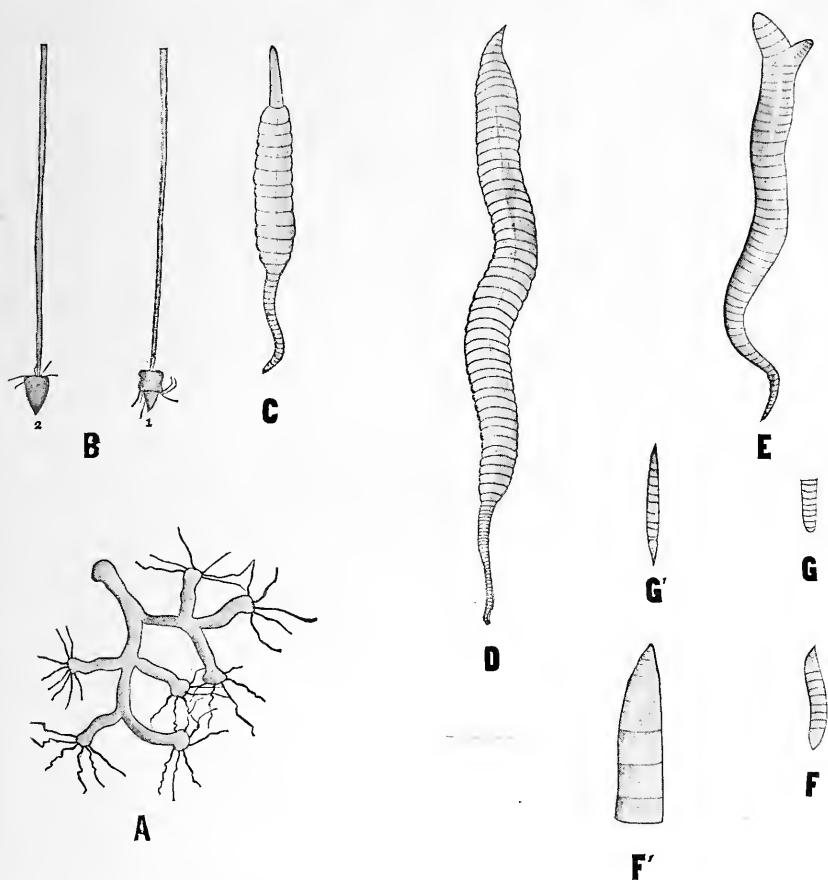


FIG. 1.— *A–B.* After Trembley. *C–G′.* After Bonnet. *A.* Seven-headed hydra made by splitting head-ends lengthwise. *B.* Illustrating the method of turning hydra inside out by means of a bristle: 1, foot being pushed through mouth; 2, completion of process. *C.* Middle piece of an earthworm (cut into three pieces) with new head and tail. *D.* Anterior part of an earthworm regenerating a new " delicate " tail. *E.* Posterior third of a worm (lumbriculus) that regenerated two heads. *F.* Middle piece of a worm (another species) cut into three pieces. It made a tail at each end. *F′.* Anterior, enlarged end (tail) of last. *G.* Small piece of a worm. *G′.* Regeneration of head and tail of same.

piece. He found that if a worm is cut into three, four, eight, ten, or even fourteen pieces, each piece produces a new worm; a new head appearing on the anterior end of each piece, and a new tail on the posterior end (Fig. 1, *G, G′*). The growth of the new head is limited in all cases to the formation of a few segments, but the new

tail continues to grow longer, new segments being intercalated just in front of the end-piece that contains the anal opening. In summer the regeneration of a new part takes place in two to three days; in winter in ten to twelve days, this difference not being due to the time of year, but to the temperature. Bonnet found that if a newly regenerated head is cut off, a new one regenerates, and if the second one is removed, a third, new one develops, and in one case this occurred eight times: the ninth time only a bud-like outgrowth was formed. In other cases a new head was produced a few more times, but never more than twelve. He thought that the capacity of a part to regenerate is in proportion to the number of times that the animal is liable to be injured under natural conditions.

Bonnet found that short pieces from the anterior or posterior end of the body failed to regenerate, and usually died in a few days. Occasionally two new heads appeared at the anterior end of a piece (Fig. 1, $E$), and sometimes two tails at the posterior end.

Another kind of fresh-water worm[1] was found that gave a very remarkable result. If it was cut in two pieces, the posterior piece produced at its anterior end, not a new head, but a new tail. Thus there is formed a worm with two tails turned in opposite directions, as shown in Fig. 1, $F$, $F'$.

Spallanzani made many experiments on a number of different animals, but unfortunately the complete account of his work was never published, and we have only the abstract given in his *Prodromo* (1768). He made a large number of experiments with earthworms of several kinds, and found that a worm cut in two pieces may produce two new worms; or, at least, that the anterior piece produces a new tail, which increases in length and may ultimately represent the posterior part of the body; the posterior piece, however, produces only a short head at its anterior end, but never makes good the rest of the part that was lost. A short piece of the anterior end fails to regenerate; but in one species of earthworm, that differs from all the others in this respect, a short anterior piece or head can make a new tail at its posterior end.[2] Spallanzani also found that if much of the anterior end is cut off, the development of a new head by the posterior piece is delayed, and, in some species, does not take place at all.

If a new head is cut off, another is regenerated, and this occurred, in one case, five times. If, after a new head has developed, a portion only is cut off, the part removed is replaced, and if a portion of this new part is cut off it is also regenerated. If a worm is split

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[1] An annelid of unknown species.

[2] This statement of Spallanzani's I interpreted incorrectly ('99), thinking that he obtained a two-tailed form as had Bonnet.

longitudinally into two pieces, the pieces die. If only a part of the worm is split longitudinally and one part removed, the latter will be regenerated from the remaining part.[1] Several contemporaries of Spallanzani also made experiments on the earthworm.[2]

Spallanzani found that a tadpole can regenerate its tail; and if a part of the new tail is cut off, the remaining part will regenerate as much as is lost. Older tadpoles regenerate more slowly than younger ones. If a tadpole is not fed, it ceases to grow larger, but it will still regenerate its tail if the tail is cut off.[3] Salamanders also regenerate a new tail, producing even new vertebræ. If a leg is cut off, it is regenerated; if all four legs are cut off, either at the same time or in succession, they are renewed. If the leg is cut off near the body, an imperfectly regenerated part is formed. Regeneration of the legs was found to take place in all species of salamanders that were known to Spallanzani, but best in young stages. In full-grown salamanders, regeneration takes place more promptly in smaller species than in larger ones. Curiously enough, it was found that if the fingers or toes are cut off, they regenerate very slowly. If the fingers of one side and the whole leg of the opposite side are cut off at the same time, the leg may be regenerated as soon as are the fingers of the other side. A year is, however, often insufficient in some forms for a leg to become fully formed. If an animal is kept without food for two months after a leg has been cut off, the new leg will regenerate as rapidly as in another salamander that has been fed during this time. If the animal is kept longer without food, it will decrease in size, but nevertheless the new leg continues to grow larger. Occasionally more toes or fewer toes than the normal number are regenerated; but as a rule the fore leg renews its four toes, and the hind leg its five toes.

In one experiment, all four legs and the tail were cut off six times during the three summer months, and were regenerated. Spallanzani calculated that 647 new bones must have been made in the new parts. The regeneration of the new limbs was as quickly carried out the last time as the first. Spallanzani also found that the upper and lower jaws of salamanders can regenerate.

If the tentacles of a snail or of a slug are cut off, they are renewed; and Spallanzani found that even if the entire head is cut off a new one is regenerated. Also other parts of the snail, as the foot, or the

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[1] There is some doubt in regard to this statement of Spallanzani's. In a letter to Bonnet he denies that this takes place in the earthworm.

[2] Spallanzani refers to the work of Ginnani, Vandelli, Vallisneri.

[3] He found that the legs of the tadpole of the frog, and of two species of toads, also have the power of regeneration.

collar, may be regenerated. The head of the slug, it was found, regenerates with more difficulty than does that of the snail.

These justly celebrated experiments of Trembley, Réaumur, Bonnet, and Spallanzani furnished the basis of all later work. Many new facts, it is true, have been discovered, and in many cases we have penetrated further into the conditions that influence the regeneration, but many of the important facts in regard to regeneration were made known by the work of these four naturalists.

### *SOME FURTHER EXAMPLES OF REGENERATION*

So many different phenomena are included at the present time under the term "regeneration," that it is necessary, in order to get a general idea of the subject, to pass in review some typical examples of the process.

The regeneration of different parts of the salamander shows some characteristic methods of renewal of lost parts. If the foot is cut off a new foot is regenerated; if more than the foot is cut off, as much is renewed as was lost. For instance, if the cut is made through the fore leg, as much of the fore leg as was removed, and also the foot, are regenerated; if the cut is made through the upper part of the leg, the rest of that part of the leg and the fore leg and the foot are regenerated. The new part is at first smaller than the part removed, although it may contain all the elements characteristic of the leg. It gradually increases in size until it has grown to the same size as the leg on the other side of the body, and then its growth comes to an end.

Other parts of the body of the salamander also have the power of regeneration. If a part of the tail is cut off, as much is renewed as has been removed; if a part of the lower or upper jaw is cut off, the missing part is regenerated; if a part of the eye is removed, a new eye is formed from the part that remains; but if the whole eye is extirpated, or the whole limb, together with the shoulder girdle, is removed, neither structure is regenerated.

In other vertebrates the power of regeneration is more limited. A lizard can regenerate its tail, but not its limbs. A dog can regenerate neither its limbs nor its tail.

It has been stated that the new limb of the salamander is at first smaller than the one removed, but it may contain all the elements of the original limb. We find this same phenomenon in other forms, and since it is a point of some theoretical interest, a few other examples may be given. If the tail of a fish that has a bilobed form is cut off near the base, as indicated in Fig. 40, *G*, there appears over the exposed edge a narrow band of new material. The new part

now begins to grow faster at two places than at intermediate points, as shown in Fig. 40, *H*. The new tail, although very short, assumes, as a result, the characteristic bilobed form. The point of special
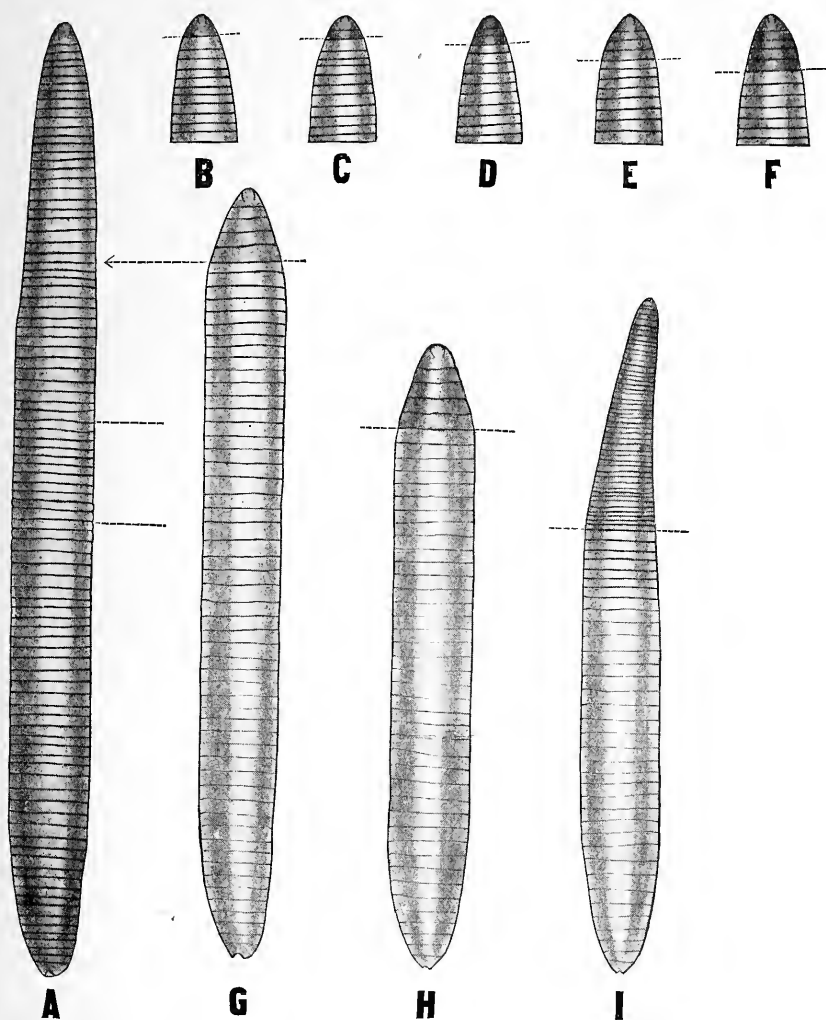


FIG. 2. — *A. Allolobophora fœtida*. Normal worm. *B–F*. Anterior ends of worms, which, after the removal of one, two, three, four, and five segments, have regenerated the same number. *G*. Anterior third cut off. Only five head-segments regenerated. *H*. Worm cut in two in middle. A head-end of five segments regenerated. *I*. Worm cut in two posterior to middle. A heteromorphic tail regenerated at anterior end.

interest is that the new material that appears over the exposed edge does not first grow out at an equal rate at all points until it reaches the level of the original fork, and then continue to grow faster in two

regions to form the lobes of the tail, but the two regions of most rapid growth are very soon established in the new tail. Subsequent growth in all parts of the new tail enlarges it to the full size.
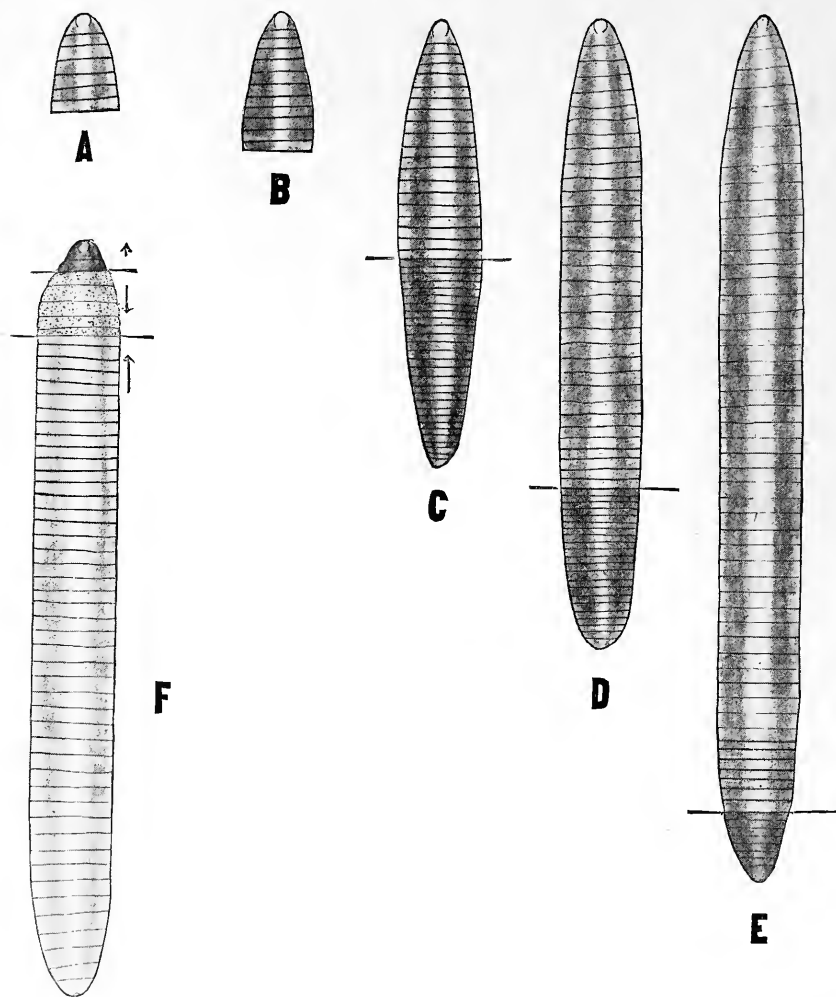


FIG. 3. — *A*, *B*. Short head-ends of *A. fœtida* that did not regenerate at posterior surface. *C*, *D*, *E*. Longer anterior pieces, that made new segments at their posterior ends. *F*. After Hazen. A piece consisting of five (3 to 7) anterior segments grafted, in a reversed position, upon the anterior end of another worm. A heteromorphic head of about two segments regenerated at the free end, which is the posterior end of the piece.

In some cases of regeneration, in which the new part is at first smaller than the part removed, the new part represents at first only the distal portion of the body, and although the new part may grow to the full size, the whole of the part removed may never come back.

This is illustrated in the regeneration of the anterior end of the earth-worm; for example, in the red-banded earthworm, or brandling (*Allo-lobophora fœtida*).[1] If one segment of the anterior end is cut off, one segment is very quickly regenerated (Fig. 2, *B*); if two segments are cut off, two come back (Fig. 2, *C*); if three segments are cut off, as many are regenerated (Fig. 2, *D*); if four are cut off, generally four come back (Fig. 2, *E*); when five are cut off, four or five come back (Fig. 2, *F*); but if six or more are cut off, only four or five are regenerated (Fig. 2, *G*). It is found in this case that a limit is soon reached beyond which fewer segments are produced than have been removed. The new segments form the anterior end or head that enlarges to the char-acteristic size; but the missing segments behind the new head are never regenerated, and the worm remains shortened throughout the rest of its life. If the reproductive region has been removed with the anterior part, new reproductive organs are never formed and the worm remains incapable of reproducing itself.

This same relation between the number of segments cut off from the anterior end and the number that is regenerated seems to hold good throughout the whole group of annelids, although the maximum number that comes back may be different in different species. Thus in lumbriculus six or seven or even eight new segments come back if more than that number have been removed.

If we examine the method of regeneration from the posterior end of a piece of an earthworm, we find that when several or many posterior segments have been removed a new part comes back, com-posed at first of a very few segments. The terminal segment contains the new posterior opening of the digestive tract. New segments are now formed just in front of the terminal segment, the youngest being the one next to the end-segment. The process con-tinues until the full complement of segments is made up (Fig. 3, *C*, *D*, *E*). Comparing these results with those described above for the anterior end, we find, in both cases, that only a few segments are at first formed, but in the posterior regeneration new segments are intercalated near the posterior end. This process of interca-lation is the characteristic way in which many annelids add new seg-ments to the posterior end, as they grow larger and longer.

Amongst the flatworms the fresh-water planarians show remark-able powers of regeneration. If the anterior end is cut off at any level, a new head is produced (Fig. 4, *C*). The new worm is at first too short, *i.e.* the new head is too near the pharynx, but changes take place in the region behind the new head that lead to the devel-opment of new material in this part. The new head is, in conse-

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[1] These experiments on the earthworm are in the main taken from my own results ('95) ('97) ('99).

quence, carried farther and farther forward until the typical relations
of the parts have been formed, when the growth in the region behind
the head comes to an end (Fig. 4, $C^1$). Similar changes take place
when the posterior end is cut off, as shown in Fig. 4, $B$, $B^1$. The new
part contains the new pharynx that is proportionately too near the
head, but the pharynx is carried farther backwards by the formation
of new material in front of it, until it has reached its typical distance
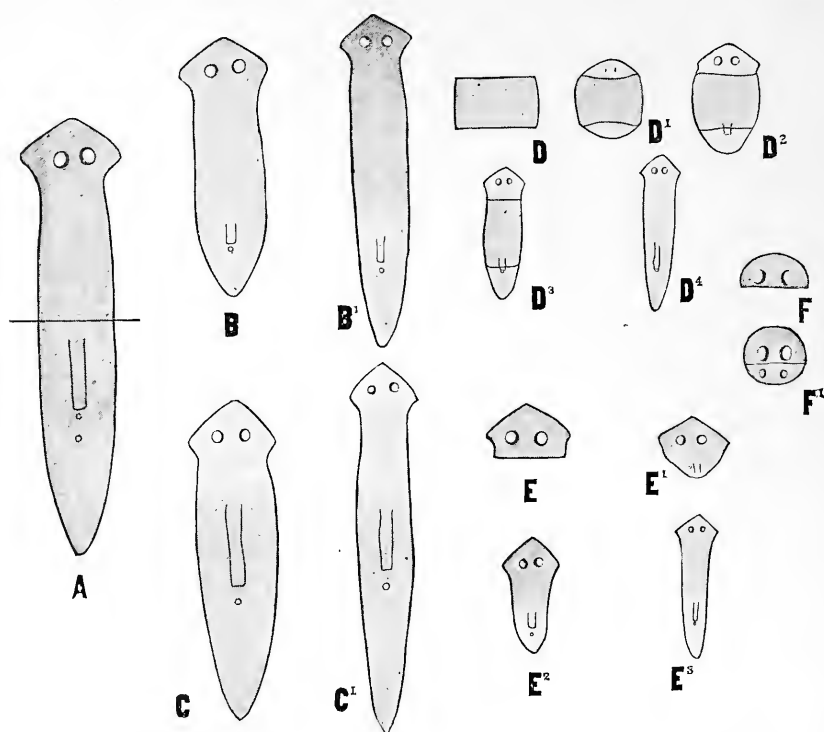


FIG. 4. — *A–E. Planaria maculata.* *A.* Normal worm. *B, $B^1$.* Regeneration of anterior half.
*C, $C^1$.* Regeneration of posterior half. *D.* Cross-piece of worm. *$D^1, D^2, D^3, D^4$.* Regenera-
tion of same. *E.* Old head. *$E^1, E^2, E^3$.* Regeneration of same. *F. P. lugubris.* Old head
cut off just behind eyes. *$F^1$.* Regeneration of new head on posterior end of same.

from the head. In these planarians the results are somewhat com-
plicated, owing to the old part changing its form, especially if the
piece is not fed; but the main facts are given above, and a more
complete account of the changes that occur will be given in another
place.

### LATERAL REGENERATION

Not only does regeneration take place in an antero-posterior direc-
tion, but in many animals also at the side. The regeneration of the
limb of the salamander is, of course, a case of lateral regeneration in

relation to the animal as a whole, but in a longitudinal direction in regard to the limb itself. Lateral regeneration of the limb would take place if the limb was split lengthwise into two parts and one of the parts removed. If the entire salamander were cut in two lengthwise, each half would most certainly die without regeneration, if for no other reason than that the integrity of the median organs is necessary for the life of the different parts. If, however, a planarian is cut lengthwise into a right and left half, each piece will complete itself laterally and make a new worm (Fig. $13\frac{1}{2}$, *A–D*). Even a narrow piece cut from the side will produce a new worm by regenerating laterally, as shown in Fig. 19, *a, b, c.* In hydra, also, a half-longitudinal piece produces a new animal, but in this case not by the addition of new material at the side, but by the cut-edges meeting to make a tube of smaller diameter. Subsequently the piece changes its form into that characteristic of hydra.

### REGENERATION OF TERMINAL PORTIONS OF THE BODY

In most of the preceding examples the behavior of the larger piece of the two that result from the operation has been described; but there are some important facts in connection with the regeneration of the smaller end-pieces. The leg, or the tail, that has been cut from the salamander soon dies without regenerating. The life of the leg can be maintained only when the part is supplied with certain substances from the body of the animal. It does not follow, of course, that, could the leg or the tail be kept alive, they would regenerate a salamander. In fact, there is evidence to show, in the tail at least, that, although it may regenerate a structure at its anterior end, the structure is not a salamander, but something else. This has been definitely shown in certain experiments with the tail of the tadpole. It is possible to graft the tail of one tadpole in a reversed position, *i.e.* with its anterior end free, on the tail of another tadpole (Fig. 54, *A–D*), or even on other parts of the body. Regeneration takes place from the free end, *i.e.* from the proximal end of the grafted tail. The new structure resembles a tail, and not a tadpole. If it be objected that the experiment is not conclusive because of the presence of the old tail, or of the use of the newly developing part, the objection can be met by another experiment. If, as shown in Fig. 56, *A*, a triangular piece is cut out of the base of the tail of a young tadpole, the cut being made so deep that the nerve-cord and notochord are cut in two, there develops from the proximal end of the tail a new tail-like structure that is turned forward, or sometimes laterally. In this case the objections to the former experiment do not apply, and the same sort of a structure, namely, a tail, is produced.

In the earthworm also we find some interesting facts connected
with the regeneration of the terminal pieces. If one, two, three,
four, or five segments are cut from the anterior end, they will die
without regenerating. Pieces that contain more segments, six to
ten, for example, may remain alive for a month or longer, but do not
regenerate (Fig. 3, *A, B*). That this lack of power to regenerate at the
posterior end is not due to the smallness of the piece can be shown
by removing from a piece of five segments one or two of its anterior
segments. These will be promptly regenerated. Another experiment
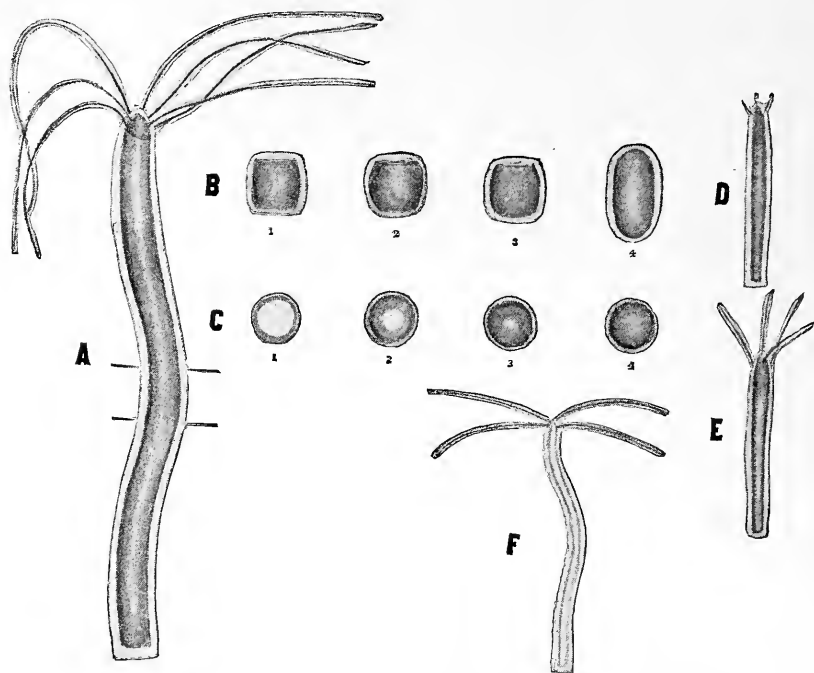


FIG. 5.—*Hydra viridis. A.* Normal hydra. Lines indicate where piece was cut out. *B*, 1-4.
Changes in a piece of *A*, as seen from the side. *C*, 1-4. Same as seen from the end. *D, E,
F.* Later stages of same piece, drawn to same scale.

has shown, however, that if these small pieces can be kept alive for a
long time, and also supplied with nourishment, regeneration will take
place at the posterior end. If, for instance, a small piece of eight or
ten segments has its anterior three or four segments cut off, and is
grafted by its anterior end to the anterior end of another worm, as
shown in Fig. 3, *F*, the piece will begin, after several months, to re-
generate at its exposed posterior end, but in the one instance in which
this experiment has been successfully carried out, a new head, and
not a tail, appeared on the exposed free end. The result is not due
to the grafting, or to the anterior position of the posterior end, but to

some peculiarity in the piece itself. We find the converse of this result in an experiment with the tail region of the earthworm, where the outcome is more clearly seen to be connected with the nature of the piece itself. If a piece less than half the length of the worm is cut off from the posterior end, there is generally formed from its anterior cut-surface, not a head, but another tail (Fig. 2, *I*). The result is similar to that described by Bonnet for one of the fresh-water annelids. A parallel case to that of the head of the earthworm is found in one of the planarians. If the head of *Planaria lugubris* is cut off just behind the eyes (Fig. 4, *F*), there is produced, at the posterior cut-edge of the head, a new head turned in the opposite direction, as shown in Fig. 4, *F*[1].

## REGENERATION BY TRANSFORMATION OF THE ENTIRE PIECE

In the regeneration of some of the lower animals, the transformation of a piece into a new animal of smaller size is brought about by a change in form of the piece itself, rather than through the production of new material at the cut-ends. If a ring is cut from the body of hydra, as shown in Fig. 5, *A*, the open ends of the ring are soon closed by the contraction of the sides of the piece, and in the course of a few hours the ring has become a hollow sphere; or, if the piece is longer, a closed cylinder. After a day or two, the piece begins to elongate, and four tentacles appear near one end (Fig. 5, *B*, *C*, *D*). The piece continues to elongate until it forms a small polyp, having the typical proportions of length to breadth (Fig. 5, *E*, *F*). It has changed into a new cylinder that is longer than the piece cut off, but correspondingly narrower. In this case there cannot be said to be a replacement of the missing parts, but rather, through the transformation of the old piece, the formation of a new whole. In planarians also the formation of a new worm from a piece involves a change in the form of the old part, as well as the addition of new material at the cut-end. If a cross-piece is cut out, as shown in Fig. 4, *D*, new material appears at the ends, but the old piece also becomes narrower and longer (Fig. 4, *D*[1]–*D*[4]). If the old head is cut off, it produces new material at its posterior end (Fig. 4, *E*, *E*[1]), and also becomes smaller
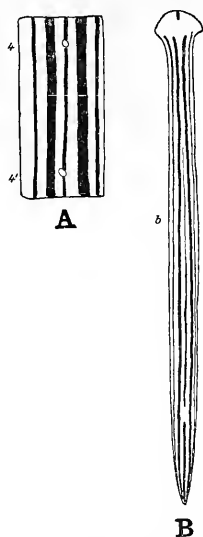


FIG. 6. — *A*. Piece of *Bipalium kewense*. Middle pigment stripe injured at two points (see circles in *A*). *B*. Regeneration of same piece.

as the new part grows larger (Fig. 4, $E^2$, $E^3$). In a land planarian, *Bipalium kewense*, a piece is transformed into a new worm, as shown in Fig. 6, $A$, $B$. In this case the old pigment stripes of the piece are carried directly over into the new worm, the piece elongating during the transformation.

A similar change takes place in pieces of unicellular animals, as best shown by cutting off pieces of stentor. If *Stentor cœruleus* is
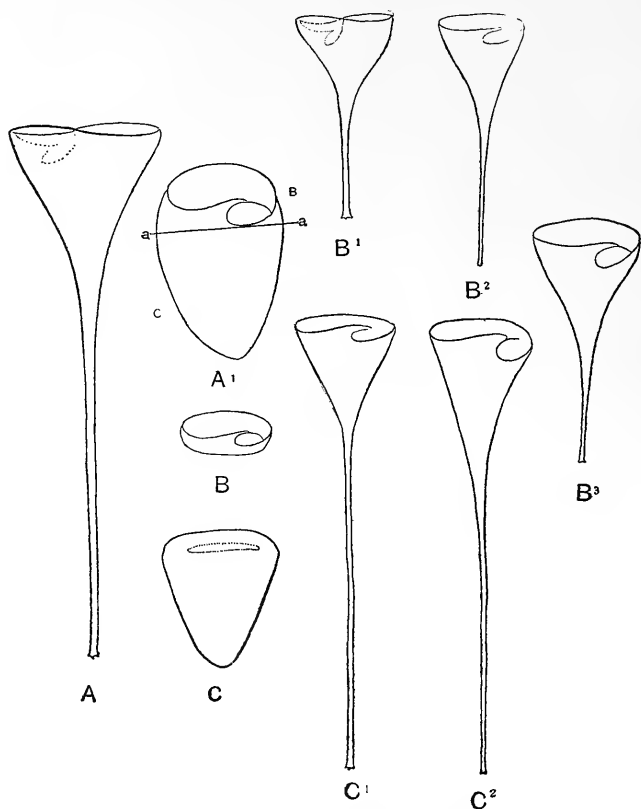


FIG. 7. — *Stentor cœruleus.*   $A$. Normal, fully expanded individual.   $A^1$. Same contracted. Line *a–a* indicates where it was cut in two.  $B$, $C$. Pieces after division.  $B^1$, $B^2$, $B^3$. Regeneration of three distal pieces ($B$) containing old peristome.   $C^1$, $C^2$. Regeneration of two proximal or foot pieces ($C$).

cut in two pieces, as indicated in Fig. 7, each piece makes a new individual of half size, but of proportionate form. The old peristome remains on the anterior piece, but becomes reduced in size as the piece changes its shape, and although it may be at first too large for the length of the new piece, it ultimately reaches a size about proportionate to the rest of the animal. The posterior piece is at first too long

for the size of the new peristome that is formed, but the latter becomes larger, until the characteristic form has been reached. The change in form of the stentor may take place in a few hours, and the result
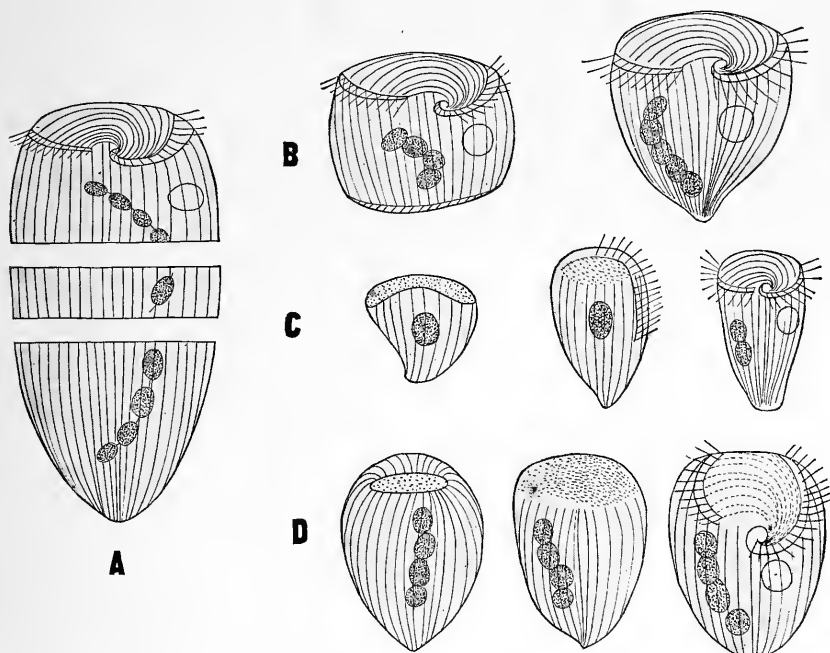


FIG. 8. — After Gruber. *Stentor cœruleus.* *A.* Cut into three pieces. *B.* This row shows regeneration of anterior piece. *C.* This row shows regeneration of middle piece. *D.* This row shows regeneration of posterior piece.

is brought about, not by the development of new protoplasm over the cut-end, but by a change of the old protoplasm into the new form. A similar experiment is shown in Fig. 8, in which a stentor was cut into three pieces, each piece containing a part of the old nucleus.

### REGENERATION IN PLANTS

In the higher plants the production of a new plant from a piece takes place in a different way from that by which in animals a new individual is formed. The piece does not complete itself at the cut-ends, nor does it change its form into that of a new plant, but the leaf-buds that are present on the piece begin to develop, especially those near the distal end of the piece, as shown in Fig. 32, *A*, and roots appear near the basal end of the piece. The changes that take place in the piece are different from those taking place in animals, but as the principal difference is the development of the new part near the end, rather than over the end, and as in some cases the

new part may even appear in new tissue that covers the end, and, further, since the process seems to include many factors that appear also in animals, we are justified, I think, in including this process in plants under the general term regeneration.
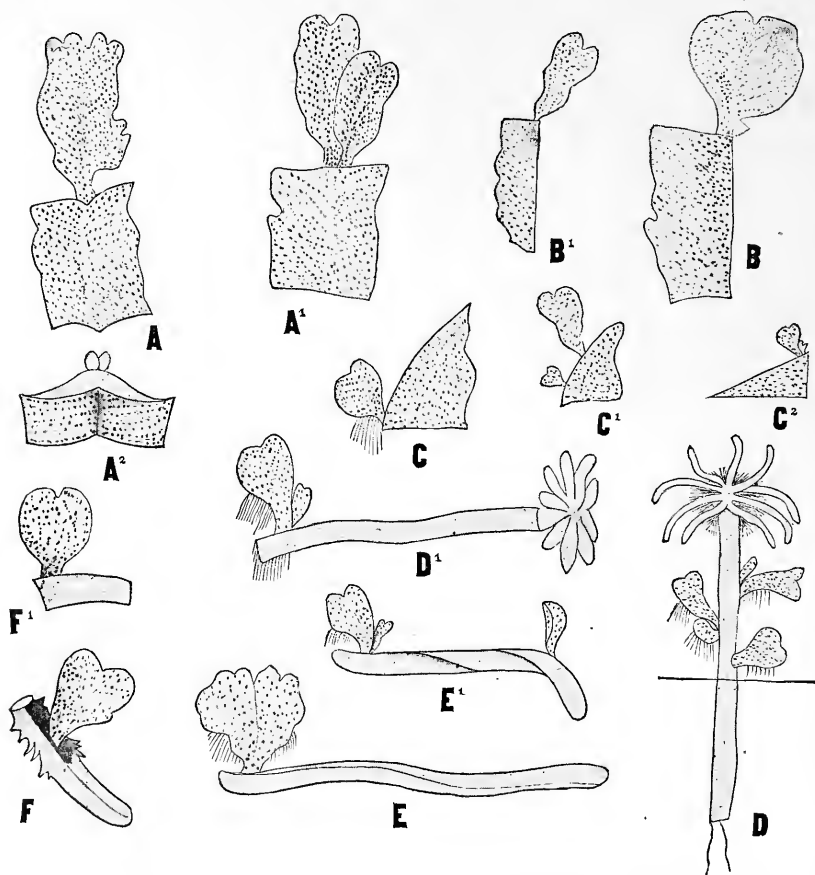


FIG. 9. — After Vöchting. *A*, *A*1, *A*2. Pieces of thallus of *Lunularia communis* regenerating at the apical end. *B*. Piece of thallus cut in two in the middle line. *B*1. Same split at side of middle. *C*. An oblique piece extending to middle line. *C*1, *C*2. Oblique pieces not extending to middle line. *D*. Fruiting stalk stuck into sand, producing new thallus above sand. *D*1. Same laid horizontally regenerating near base. *E*. Same with fruiting head cut off. Regenerating at base. *E*1. Twisted piece regenerating at two points. *F*. Piece of ray of head regenerating near base. *F*1. Same with distal end of ray cut off. Also regenerating at base.

In the lower plants, such as the mosses, the liverworts, the moulds, and the unicellular forms, regeneration also takes place. Vöchting has shown that pieces from any part of the thallus of a liverwort [1] produce new plants. If a cross-piece is cut off, there appears a small

[1] *Lunularia vulgaris.*

outgrowth from the middle of the anterior cut-edge, as shown in Fig. 9, $A$, $A^2$, that gradually enlarges to form a new thallus. It will be seen from the figures that the whole anterior edge does not grow forward, but a new thallus arises from a group of cells at, or near, the anterior edge. These cells are the least-differentiated cells in the piece, and have softer cell walls than have the other cells.
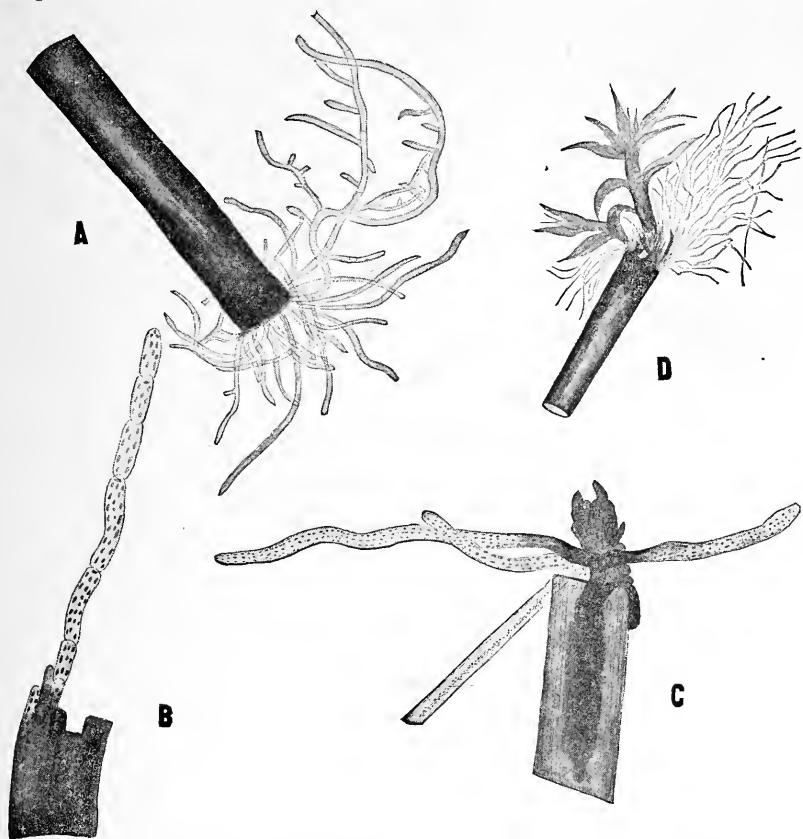


FIG. 10.— After Pringsheim. *A*. A piece of seta of sporophore of *Hypnum cupressiforme*, sending out protonema-threads. *B*. Longitudinal section of a piece of the seta of sporophore of *Bryum cæspitosum*. *C*. Piece of same of *Hypnum cupressiforme*. Moss-plant arising from new protonema. *D*. Piece of same of *Hypnum serpens* with protonema and moss-plant arising from it.

Pringsheim has shown that if a piece of the stalk of the sporangium of certain mosses is cut off, it produces at its ends thread-like outgrowths which are like the protonema-stage of the moss, and from this protonema new moss-plants may arise (Fig. 10, $A$, $B$, $C$, $D$).

Braefeld has obtained a somewhat similar result in one of the moulds, in which a piece of the sporangium stalk gives rise to a mycelium from which new sporangia may be produced.

c

## REGENERATION IN EMBRYOS AND EGGS

Regeneration takes place not only in adult organisms, but also in embryos, and larvæ of many animals. It is often stated that the power of regeneration is more highly developed in embryos than in adults, but the facts that can be advanced in support of this view are not numerous. One of the few cases of this sort known to us is that of the leg of the frog, that does not regenerate, while the leg of the tadpole is capable of regenerating.
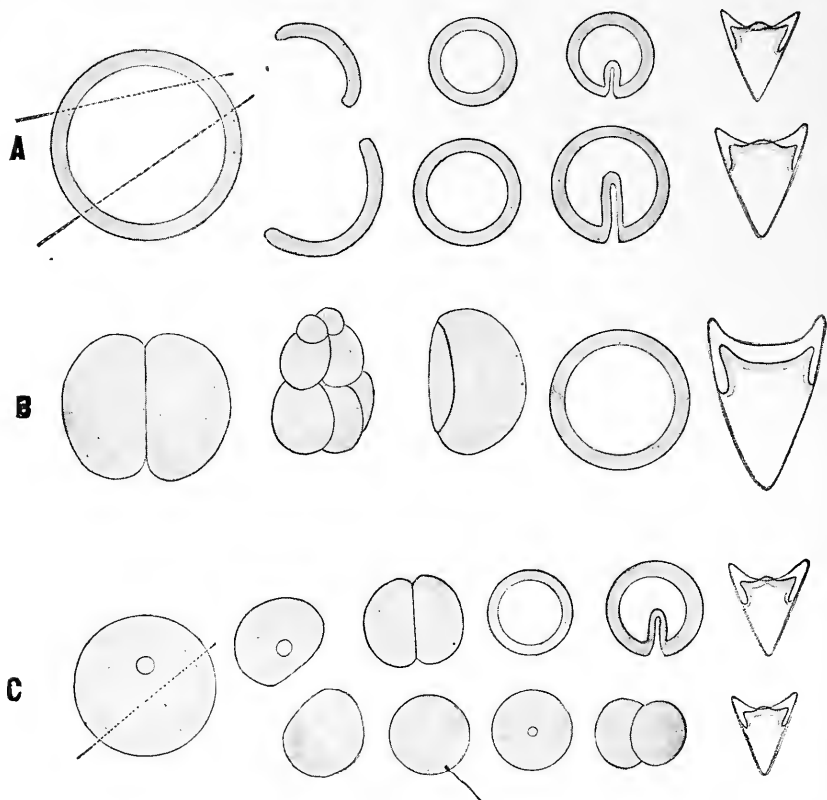


FIG. 11.—*A.* Blastula of Sea-urchin. Dotted lines indicate where pieces of wall were cut off. To the right are shown stages in the development of these pieces. *B.* Two-cell stage of egg of sea-urchin. One blastomere isolated. Its development shown in figures to right of *B.* *C.* Fertilized but unsegmented egg. Dotted line indicates where it was cut in two. Upper row of figures to right shows development of nucleated piece; lower row shows the fertilization and development of non-nucleated piece.

The early stages in the development of the sea-urchin, or of the star-fish, may be taken to illustrate the power of regeneration in embryos. If the hollow blastula of the sea-urchin is cut into pieces (Fig. 11, *A*), each piece, if not too small, may produce a new blastula. The

edges of the piece come together, and fuse in the same way in which a piece of hydra closes. A new hollow sphere of small size is formed, which then passes through the later stages of development as does the whole normal blastula.

Still earlier stages of the sea-urchin, or of the starfish, have the power of producing embryos if they are cut into pieces. If the segmenting egg is separated into a few parts, each part will continue to develop. Even the first two blastomeres or cells will, if separated, produce each a whole embryo (Fig. 11, *B*). The power of development of a part does not even end here, for, if the undivided, fertilized egg is cut into pieces, the part that contains the nucleus will segment and produce a whole embryo (Fig. 11, *C*, upper row). If the egg is cut in two or more pieces before fertilization, and then each part is fertilized, it has been found that not only the nucleated, but even the non-nucleated fragments (if they are entered by a single spermatozoon) may produce embryos (Fig. 11, *C*, lower row).

It may be questioned whether the development of parts of the embryo, or of the egg, into a whole organism can be included in the category of regenerative processes. There are, it is true, certain differences between these cases and those of adult forms, but as there are many similarities in the two cases, and as the same factors appear in both, we cannot refuse, I think, to consider all the results from a common point of view.

### PHYSIOLOGICAL REGENERATION

Finally, there are certain normal changes that occur in animals and plants that are not the result of injury to the organism, and these have many points in common with the processes of regeneration. They are generally spoken of as processes of physiological regeneration. The annual moulting of the feathers of birds, the periodic loss and growth of the horns of stags, the breaking down of cells in different parts of the body after they have been active for a time, and their replacement by new cells, the loss of the peristome in the protozoon, stentor, and its renewal by a new peristome, are examples of physiological regeneration. This group of phenomena must also be included under the term "regeneration," since it is not sharply separated from that including those cases of regeneration after injury, or loss of a part, and both processes appear to involve the same factors.

### DEFINITION OF TERMS

The older writers used such terms as "replacement of lost parts," "renewal of organs," and "regeneration" to designate processes similar to those described in the preceding pages. The term regen-

eration has been for a long time in general use to include all such phe-
nomena as those referred to, but amongst recent writers there is some
diversity of opinion as to how much is to be included in the term, and
the question has arisen as to the advantage of applying new names
to the different kinds of regeneration.   There can be little doubt of
the advantage, for the sake of greater clearness, of the use of different
terms to designate different phenomena, but I think that there is at
the same time the need of some general term to cover the whole field,
and the word regeneration, that is already in general use, seems to
fulfil this purpose better than any other.

Roux[1] points out that Trembley, and later Nussbaum, showed
that a piece of hydra regenerates without the formation of new mate-
rial.   Roux adds that since during development the piece takes no
nourishment, the *regeneration* must be brought about by the rearrange-
ment of the cells present in the piece.[2]   The change may, or may
not, involve an increase in the number of the cells through a process
of division.   In consequence of this method of development a re-dif-
ferentiation of the cells that have been already differentiated takes
place.   This process of regeneration, Roux points out, is very similar
to the " post-generation " of the piece of the blastula of the sea-urchin
embryo, and he concludes that " regeneration may be brought about
entirely, or very largely, through the rearrangement and re-differen-
tiation of cells without any, or with very little, proliferation taking
place."   In the adults of higher animals regeneration by prolifera-
tion preponderates, but rearrangement and re-differentiation of cells
occur in all processes of regeneration, even in higher vertebrates.
The two kinds of regeneration that Roux distinguishes are, he says,
essentially quantitative.[3]

[1] Gesammelte Abhandlungen, No. 27, p. 836.

[2] The fact that the piece does, or does not, take in food has no bearing on the question,
since many animals that do not feed while the regeneration is going on produce new cells to
form the new part.

[3] These two kinds of regeneration are post-generation and regeneration proper.   The
distinction that Roux attempts to make between these two processes is to a certain extent
artificial and rests at present on a very unsafe basis, at least in so far as the post-generation
of the frog's embryo is taken as a representative case of this process.   Roux states that in
the process of *regeneration* the injured tissues produce each their like in the new part, while
in the process of *post-generation* of the frog's egg the new cell-material arises in part from
the nuclei and yolk-material of the injured half and in part through the accidental posi-
tion of the nuclear material of the uninjured half.   In order more fully to understand this
distinction the original description of the process of post-generation given by Roux in his
account of the development of half embryos of the frog's egg must be referred to.   In later
papers Roux pointed out that the missing half of the frog embryo, as well as of other forms,
may be post-generated without any new material appearing at the open side of the embryo.
It is unfortunate, I think, that the original term should have been extended to include these
other processes that do not partake of the nature of post-generation as at first defined, but
are more like the true process of regeneration as described by Roux.

Barfurth[1] has defined regeneration as "the replacement of an organized whole from a part of the same." If the part is given by nature, there is a process of physiological regeneration; if the part is the result of an artificial injury, the process is one of pathological regeneration. Barfurth includes in the latter category the production of a new, entire individual from a piece, as in hydra; regeneration by proliferation, as in the earthworm; and also the development of pieces of an egg or of an embryo.

Barfurth's definition of regeneration is unsatisfactory, since an egg is itself a portion of an organism that makes a new whole, and this sort of development is not, of course, as he himself points out, to be included in the term regeneration. Nor does the use of the word "replacement" save the definition, since in many cases the kind of part that is lost is not replaced. The use of the word "pathological" to distinguish ordinary regeneration from physiological regeneration is, I think, also unfortunate, since it implies too much. There is nothing necessarily pathological in the process, especially in such cases as hydra, or as in the development of a piece of an egg where the piece is transformed directly into a new organism. Furthermore, in those cases in which (as in some annelids and planarians) a new head is formed after or during the process of natural division, there is little that suggests a pathological process; and in this instance the regeneration takes place in the same way as after artificial section.

Driesch, in his *Analytische Theorie*, states that Fraisse and Barfurth have established that during regeneration each organ produces only its like. Driesch defines regeneration, therefore, as the re-awakening of those factors that once more bring into play, by means of division and growth, the elementary processes that had ceased to act when the embryonic development was finished. This is regeneration in the restricted sense, but Driesch also points out that this definition must be enlarged, since, when a triton, for example, regenerates its leg, not only does each tissue produce its like, but later a reconstruction and differentiation takes place, so that a leg and foot are formed, and not simply a stump containing all of the typical tissues. Driesch holds that regeneration should include only those cases in which a *proliferation* of new tissue precedes the development of the new part, and suggests that other terms be used for such cases as those of pieces of hydra, pieces of the egg, etc., in which the change takes place in the old part without proliferation of new tissue. It seems to me unwise to narrow the scope of the word regeneration as Driesch proposes, for it has neither historical usage in its favor, nor can we make any fundamental distinction between cases in which proliferation takes place and those in which it does not. As will be shown later,

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[1] Ergebnisse der Anatomie und Entwickelungsgeschichte. 1891–1900.

the factors that are present in the two cases appear to be in large part the same, and while it may be convenient to put into one class those cases in which proliferation precedes the formation of the new organs, and into another class those cases in which the change takes place without proliferation, yet, since the distinction is one of subordinate value, it is necessary to have one word to include both groups of cases ; and no better word than regeneration has, I think, been as yet suggested.

Driesch has made use of two other descriptive terms. The word " reparation " is used to describe the development of the hydranth of tubularia. The new hydranth is formed in this case out of the old tissue at the end of the piece (Fig. 20, *A*). The change appears to be the same as that which takes place in a piece of hydra, etc. The word " reparation " does not seem to me to express very satisfactorily this sort of change, or sharply separate it from those cases in which the animal is *repaired* by adding what has been taken away ; but in this latter sense Driesch does not use the term. I have not made use of the word, in general, except as applied to Driesch's work.

Another term, "regulation," used by Roux,[1] and also by Driesch and others, is used in a sort of physiological sense to express the *readjustments* that take place, by means of which the typical form is realized or maintained. By inference we may extend the use of the word to include the changes that take place in the new material, that is proliferated in forms that regenerate by this method. Driesch uses this term, regulation, to include a much more general class of phenomena than those included in the term regeneration, as for instance, the regulation of metabolism and of adaptation, etc. One of the subdivisions of the term regulation is called "restitution." This word also is used where I should prefer to use the word regeneration as a general term, and the word reorganization when reference is made to the internal changes that lead to the production of a typical form.

Both Roux and Driesch also speak of " self-regulation," by which is meant, I suppose, that the changes taking place are due to readjustments in the part itself, and are not induced by outside factors. The expression " self-regulation " is not, I think, a very happy one, since all change is ultimately dependent upon a relation between inside and outside conditions.

Hertwig[2] defines regeneration as the power of replacement of a part of the organism. He states that in all cases the beginning of the process is the same, viz. the appearance of a small protuberance composed of cells, that is the rudiment of the new part. It is evident

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[1] As used in connection with other terms, see his Ges. Abhandl., Vol. II, page 41.
[2] Die Zelle und die Gewebe.

that Hertwig has taken into account only one side of the process. Those cases in which a rearrangement or reorganization takes place in the old part are not even considered.[1]  Goebel[2] points out that in plants the fully formed cells are, as a rule, incapable of further growth after they have once served as a basis of an organ of the body, but often some of the cells may remain in a latent condition, and grow again, when the intercellular interactions are disturbed.  This is the case, he thinks, in regeneration.  Goebel speaks of regeneration by means of adventitious buds in those cases in which the buds had not previously existed before the removal of the part.  In those cases in which the buds are in existence before the piece is removed, as in the leaves of Asplenium, Begonia, etc., the development is not the result of regeneration, Goebel thinks, but the buds represent a stage in the development of the species.  It may be pointed out, however, that it is certainly a remarkable fact that often the conditions that lead to the unfolding of an existing bud are the same as those that lead to the development of a new bud.

The preceding account will suffice to illustrate some of the principal ideas that are held in regard to the process of regeneration. Since many new facts have come to light in the last few years, it may not be amiss to point out what terms will be used in the following pages to include each kind of process.

The word " regeneration " has come to mean, in general usage, not only the replacement of a lost part, but also the development of a new, whole organism, or even a part of an organism, from a piece of an adult, or of an embryo, or of an egg.  We must include also those cases in which the part replaced is less than the part removed, or even different in kind.

At present there are known two general ways in which regeneration may take place, although the two processes are not sharply separated, and may even appear combined in the same form.  In order to distinguish broadly these two modes I propose to call those cases of regeneration in which a proliferation of material precedes the development of the new part, " epimorphosis."  The other mode, in which a part is transformed directly into a new organism, or part of an organism without proliferation at the cut-surfaces, " morphallaxis."

In regard to the form of the new part, certain terms may be used that will enable us to characterize briefly different classes.  When the new part is like that removed, or like a part of that removed, as when a leg or a tail is regenerated in a newt, the process is one of " homo-

[1] Hertwig's description of the method by which a piece of hydra makes a new one shows that he did not understand the kind of change that takes place in this animal.

[2] Organographie der Pflanzen, '98.

morphosis."[1]   Under this heading we may distinguish two cases, in one
of which the entire lost part is at once, or later, replaced — holomorpho-
sis; in the other the new part is less than the part removed — mero-
morphosis.   When the new part is different from the part removed the
process has been called by Loeb "heteromorphosis," but there are at least
two different kinds of processes that are covered by this definition.
In one case the new part is not only different from the part removed,
but is also an organ that belongs to a different part of the body (or it
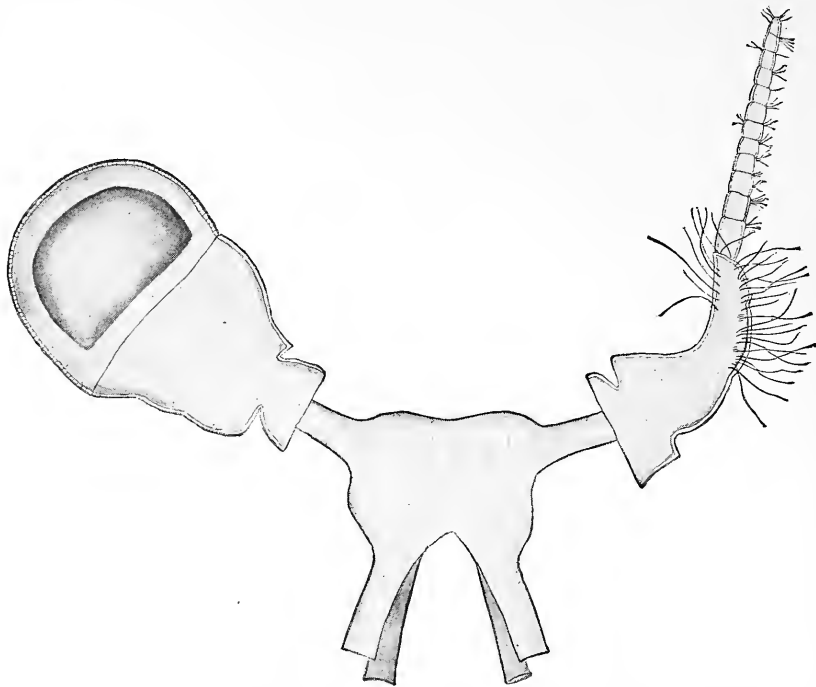


FIG. 12. — After Herbst.   Diagram showing brain, eye, and "heteromorphic" antenna (in place
of eye of one side) of palæmon.   The animal had lived in a dark aquarium for five months.

may be unlike any organ of the body).   This we may call "neomor-
phosis."   As an illustration of this process may be cited the develop-
ment of an antenna, when the eye of a crab or of a prawn is cut off
near the base (Fig. 12); and as an example of an organ different in
kind from any organ of the same animal, may be cited the case of
*Atyoïda potimirum*, in which the new leg is unlike any other leg on
the body.   The name "heteromorphosis" can be retained for those
cases in which the new part is the mirror figure of the part from
which it arises, or more generally stated, where the new part has

[1] This term is used by Driesch in his *Analytische Theorie*.

its axes reversed as compared with the old part. As an example of this may be cited the development of an aboral head on the posterior end of a piece of the stem of Tubularia (Fig. 15, *B*), or the development of a tail at the anterior end of a posterior piece of an earthworm (Fig. 2).

The term "physiological regeneration" I shall use in the ordinary sense to include such changes as the moulting and replacement of the feathers of birds, the replacement of teeth, etc., — changes that are a part of the life-cycle of the individual. In some cases it can be shown that these processes are closely related to ordinary regeneration, as when a feather pulled out is formed anew without waiting for the next moulting period, and formed presumably out of the same rudiment that would have made the new feather in the ordinary moulting process.

It is sometimes convenient to contrast the process of physiological regeneration with all other kinds. The use of the term "pathological regeneration" for the latter seems to me, as has been said, unsatisfactory. The two terms proposed by Delage,[1] viz. "regular regeneration" and "accidental regeneration," have certain advantages, although there is nothing accidental, or at least occasional, in regard to the process itself, as it is entirely regular, although it may only occur after an accident to the animal. The term "regular regeneration" is, I think, more satisfactory than "physiological regeneration," but the latter has the advantage that it has come into current use. For what is known as pathological or accidental regeneration, I propose the term "restorative regeneration," and I shall continue to use the term "physiological regeneration" as generally understood.

[1] Delage, *Y. La Structure du Protoplasma*, etc., '95.

# CHAPTER II

## THE EXTERNAL FACTORS OF REGENERATION IN ANIMALS

THERE is a constant interchange of material and of energy that takes place between a plant or an animal and its surroundings, and this interchange may be influenced by such physical conditions as temperature, light, gravity, etc., or by such chemical conditions as the composition of the atmosphere or of the water surrounding the organism. We can study the process of regeneration either by keeping the regenerating organism under the same conditions that it is subject to in its natural environment, or else we can change the surrounding physical or chemical conditions. In this way we can determine how far the regeneration is affected by external changes, and how far it is independent of them. If a change in the external conditions produces a definite change in the regeneration, then the new condition is called an external factor of regeneration.

### TEMPERATURE

That the rate at which regeneration takes place can be influenced by temperature has been shown by Trembley, Spallanzani, Bonnet, and by many more recent writers. In fact, so familiar is the process to every one who has studied regeneration, that it is usually taken for granted that such is the case.

In general it may be stated that the limits of temperature under which normal growth may take place represent also the limits of temperature for regeneration. Lillie and Knowlton ('97) have determined the limits of temperature within which regeneration takes place in *Planaria torva*. The worm was cut in two transversely through the pharynx, and the time required at different temperatures to produce a new head on the posterior piece was recorded. The lowest temperature at which regeneration was found to take place was 3° C. Of six individuals kept at this temperature only one regenerated at all, and in this one the eyes and brain were still incomplete after six months. The optimum temperature, or at least that at which regeneration takes place most rapidly, was found to be 29.7° C.; a new head developed in 4.6 days at this temperature. At 31.5° C.

regeneration was slower, requiring 8.5 days to make a new head. At 32° C. incomplete regeneration sometimes took place, but death occurred in about six days. At 33° C. regeneration was very slight, and the animals died within three days. At 34° C., and above this point, no regeneration took place, and death soon occurred.

In *Hydra viridis*, Peebles ('98) has found that regeneration is quicker at 26°–27° C. than at 28°–30° C. At the former temperature regeneration takes place in 48 hours. If kept at 12° C. pieces may regenerate in 96 hours, but not all the pieces had regenerated in this case until 168 hours.

### INFLUENCE OF FOOD ON REGENERATION

While the growth of an animal or of a plant is, in most cases, and, of course, within certain limits, directly connected with the amount of food that is obtainable, nevertheless extensive regeneration may take place in an animal, or part of an animal, entirely deprived of food. In this case the material for the new part is derived from the excess of material in the old part, and not only surplus food material, but even the protoplasm itself appears to be drawn upon to furnish material to the new part. The relation between regeneration and the amount of food present in the old part is well shown by experiments with planarians. If a planarian is kept for several months without food, it will decrease very much in size. In fact, the volume of a starved worm of *Planaria lugubris* compared with that of a fully fed individual may be only one-thirteenth of the latter (Fig. 13, *A*, *B*). If a starved worm is cut in two pieces, each piece will regenerate, although less quickly than in a well-fed worm. The new part will continue to increase in size at the expense of the old piece that is already in a starved condition. On the other hand, an excess of food does not necessarily produce a hastening of the regeneration, for, as Bardeen



FIG. 13.— Drawn by N. M. Stevens. *A*. Large well-fed individual of *Planaria lugubris*. *B*. Same after being kept without food for 4 mos. 13 days. Both drawn to same scale.

('01) has shown, worms that have been for several days without food may regenerate more quickly than worms that have been fed just before they were cut into pieces.

The growth of the new part at the expense of the old tissues is a phenomenon of the greatest importance, an explanation of which will involve, I think, the most fundamental questions pertaining to

growth.   The results show that growth is connected with a structural factor, and is not simply a physiological phenomenon, although no doubt physiological factors are involved.   But the physiological factors that are here at work seem to be different from what is ordinarily understood; for the fact that a tissue that is slowly starving to death should be reduced still further, and at a more rapid rate, in order to supply material to a new part, is certainly a remarkable phenomenon.
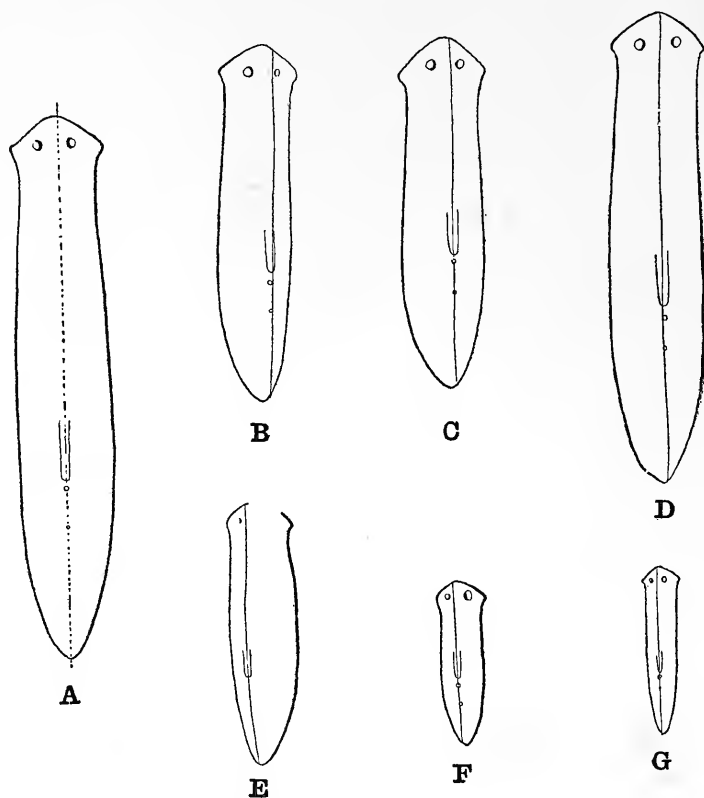


FIG. 13½. — *Planaria lugubris*.   Dotted line indicates where the worm was cut in two lengthwise. Upper three figures show how a half, that is being fed, regenerates.   Lower three figures show other half kept without food.

At present we are not in a position to offer any explanation that rests on observation, or experiment, as to how the transfer of material takes place, or as to how the new tissue manages to get hold of the material from other parts.   It is possible to protect the old part to a large extent by keeping the regenerating piece well supplied with food.   If a well-fed planarian is cut in two along the middle line of the body as indicated in Fig. 13½, *A*, there develops, in the course of five or six days after the operation, new material along the cut-side of each

piece, and a new pharynx appears at the border between the old and the new parts. If one of the pieces is fed at intervals, it is found that the new part grows more rapidly than does the new part in the piece without food. The old tissue in both pieces has shortened somewhat after the operation, and has also decreased somewhat in size as the first new material developed along the cut-side, but in the piece that is fed the old half begins to increase again until it reaches its former size, and may even surpass the latter. A large full-sized worm is produced from this piece, as shown in Fig. $13\frac{1}{2}$, *B, C, D*. In the starved piece the old part continues to grow small, due to the lack of food and also to the increase in the new side. This increase takes place very slowly, but ultimately a small symmetrical worm may be produced, as shown in Fig. $13\frac{1}{2}$, *E, F, G*. It will be seen that the starved piece needs to produce relatively less and less new material in order to become symmetrical, because as the old material diminishes, the pharynx comes to lie nearer to the middle line.

## *EFFECT OF LIGHT ON REGENERATION*

Although few experiments have been made to test the effect of light on regeneration, it is certain that in many cases light has no effect on the process, neither as to the quality nor the quantity of the result. In one form, a tubularian hydroid, *Eudendrium racemosum*, it has been shown by Loeb that the regeneration of the hydranth takes place only when the animal is exposed to light. When a colony of eudendrium is brought into the laboratory and placed in an aquarium, the hydranths soon die; but if the colony is kept in a lighted aquarium, new hydranths are regenerated in a few days. If, on the other hand, the colony is kept in the dark, new hydranths do not appear; but if it is brought back again into the light the hydranths appear. In one experiment one lot of pieces was kept in diffuse daylight, and another lot in the dark. The former produced fifty new hydranths in a few days; those in the dark had not made any hydranths after seventeen days. They were then brought into the light, and in a few days several hydranths had developed on each piece.

Loeb also tried the effect of different colored light on the regeneration of eudendrium. Dishes containing pieces of the hydroid were put into a box that was covered by colored glass plates. Pieces subjected to dark red and to dark blue light gave the following results. The old hydranths, as is generally the case, were absorbed in the course of three days. The first new hydranths appeared in the blue light on the fourth day, and during the following days the hydranths in this lot steadily increased. Eight days after the beginning of the

experiment there were eighty hydranths under the blue glass, but not one had developed in the red light. On the ninth day the red glass was replaced by a dark blue one. Two days later hydranths began to appear, and on the following day thirty-two hydranths had appeared, and in a few days more as many as sixty had developed.[1] Loeb concluded that only in the more refrangible (blue) rays does the regeneration of the hydranth take place, while the less refrangible (red) rays act as darkness does.[2] This hydroid is the only animal yet found that shows the effect of light on regeneration, and it is interesting to find that it is one of the few animals known in which light has an influence on the growth, if the heliotropism, or turning towards the light, of the hydranth is looked upon as a phenomenon of growth.

There is another series of experiments made to test the effect of light on regeneration, which gave, however, negative results. Herbst observed that when the eye of certain crustacea[3] is cut off, sometimes an eye and sometimes an antenna is regenerated. A number of individuals from which the eyes had been removed were kept in the light, and others in the dark, in order to see if the presence or absence of light is a factor in determining the kind of regeneration that takes place. It was found that as many individuals regenerated eyes in the dark as in the light. It was discovered later by Herbst and myself, independently, that, when the end only of the eye-stalk is cut off, an eye regenerates, but when the eye-stalk is cut off at the base, an antenna regenerates. The difference in the result has therefore no connection with the presence or absence of light.

### GRAVITY

The only case known amongst animals, in which regeneration is influenced by the action of gravity,[4] is that of the hydroid *Antennularia antennina*. This hydroid lives attached to the bottom of the sea several metres below the surface. The hydroid consists of a single, vertical, central stem, or axis, with two or four series of lateral branches along which the hydranths arise (Fig. 14, *A*). The stem is attached by so-called stolons, or roots. In its normal growth at the free end the hydroid has been shown by Loeb to exhibit marked geotropic changes. If, for instance, the stem is bent over to one side the new growth that takes place at the apex of the stem directs the new part upwards in a vertical direction.

If pieces are cut from the stem of antennularia and suspended in

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[1] The dark red glass was fairly monochromatic; the dark blue let a trace of red light through.

[2] The same difference was found in this form in regard to heliotropism.

[3] Palæmon and Sicyonia.

[4] The regeneration of the lens of triton may also be affected by gravity.

the water, regeneration takes place at the cut-ends. If a piece is suspended with its apical end upwards (Fig. 14, *B*), a new stem develops at the upper cut-end, and new roots from the lower cut-end. If a piece is suspended with its basal end upwards (Fig. 14, *C*), there is formed at its upper (basal) end a new stem with its branches also slanting upwards as shown in the figure. Roots appear at the
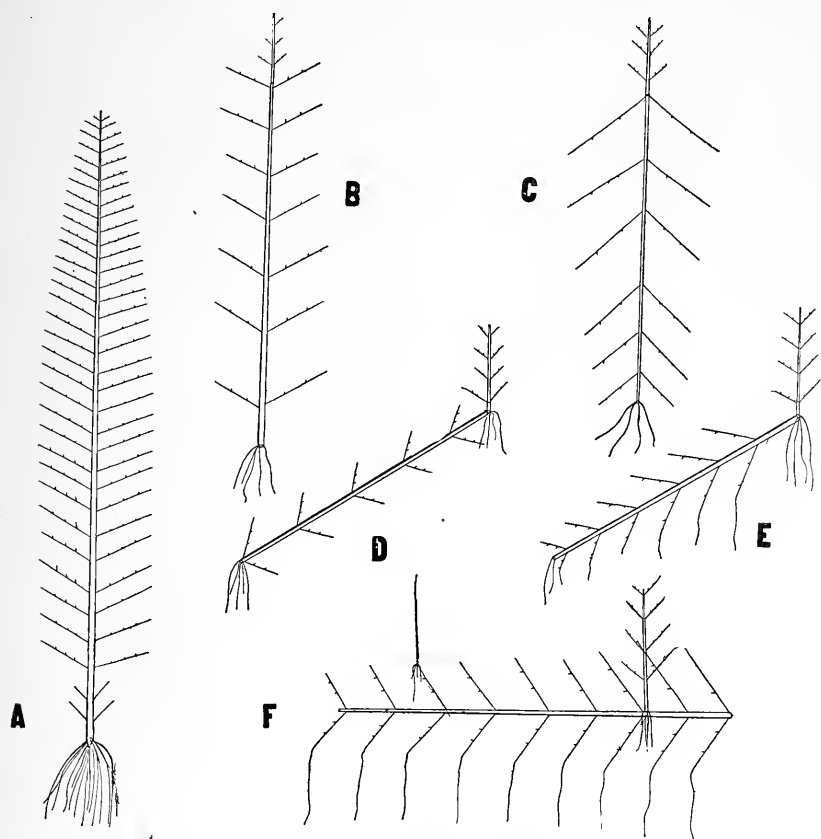


FIG. 14. — After Loeb. Normal stalk of *Antennularia antennina*. *B*. Piece regenerating in vertical, normal position. *C*. Piece regenerating in inverted position. *D*. Piece regenerating in inclined, vertical position. *E*. Piece regenerating in inclined, inverted position. *F*. Piece regenerating in horizontal position.

lower (apical) end. Since gravity is the only force that acts in a vertical direction under the conditions of the experiment, Loeb concluded that it plays an important rôle in determining the kind of regeneration that takes place. Its action is of such a nature that a new stem develops from the upper cut-end, and roots from the lower end, regardless of whether the upper end is the basal or the apical end of the piece. Similar results are also obtained, according to

Loeb, if the pieces are suspended obliquely. In a piece of this sort, it is found that new stems arise along the upper surface of the old stem, and roots from the lower surface as well as from the lower cut-end (Fig. 14, *D*, *E*). If a piece of the stem is placed horizontally on the bottom of an aquarium, the branches that come off from the under surface of the stem begin to grow downwards at their ends, and where they come in contact with a solid body they fasten themselves to it, thus showing that they are true roots (Fig. 14, *F*). One or more stems may arise from the upper side of the main stem. These stems grow vertically upwards, and produce lateral branches. Only in one case did a new stem, or stem-like structure, arise from one of the vertical branches, as shown to the left in Fig. 14, *F*.

Loeb found it also possible to change the character of the growth of the apex of the normal stem and to transform it into a root. A long piece of the hydroid was cut off and suspended vertically with the basal end upwards. From the upper end a new stem began to grow, and then the entire piece was reversed, so that the new stem pointed downwards. Under these circumstances the young stem did not bend around and begin to grow upwards, as a young plant might have done, but it ceased to grow as a stem, and at its apex one or more roots developed. Loeb concludes: "I cannot imagine by what means the place of the formation of organs in antennularia is determined in connection with the orientation of the animal except by means of gravity."

The response of antennularia to the action of gravity is, I think, conclusively demonstrated by Loeb's results, but that the phenomenon may be complicated by other factors is shown, I think, by the following experiments. Driesch found that if pieces of antennularia are cut off and placed between horizontal plates, so that both ends are free, roots are produced by the basal end.[1] If the basal end with its new roots is cut off, new roots may appear, but sometimes a thin stem also. If the end is again cut off, a larger stem, and also one or two roots, may appear, and if the operation is repeated again only a stem is formed. The factor that brings about this change is not shown by the experiment. The piece had been kept in a horizontal position throughout the whole time. The apical end died in most cases without producing roots, but it is not stated whether or not roots appear on the stem between the plates of glass. If they develop they may affect the result, as certain experiments that I have made seem to show.

In my experiments, made at a different time of year from that at

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[1] Driesch does not give in his paper ('99) the position of the hydroids, or the method of the experiment, but I can supply the details given above from a personal communication from Driesch.

which Loeb's experiments were made, pieces of the stem were sus-
pended vertically, — some with the apical end upwards, others with the
basal end upwards. In nearly all cases roots were formed by both
the upper and lower ends. In a few cases, in which the apical end
was upwards, a new stem developed at that end. Pieces suspended
in a horizontal position also produced roots at both ends. After
removing the ends with their new roots from the pieces suspended
vertically, I found that roots again appeared at both ends in nearly
every case. The difference between these results and those of Loeb
may be due to the time of the year at which the experiments were
made, or possibly to some other difference, but the results show that
the response to gravity is not always so constant as Loeb's results
indicate.

In a few cases in my experiments the basal end of the hydroid was
left attached to the stem on which it had grown, and the piece was
put into the same aquarium used for the preceding experiments. In
those pieces that lay on the bottom of the aquarium, with the stem
standing vertically, a new shoot, and not new roots, appeared on the
upper end. Other pieces were hung at the top of the water of the
aquarium with the stem turned downwards, and the basal, attached
end of the piece upwards. These pieces produced neither a stem nor
roots from the apical end. The results show that the presence of
roots at one end has an influence on the regeneration at the other
end. The same thing was shown in one case in which a short piece
sank to the bottom of the dish and, developing roots at its basal end,
became fixed : a stem grew out of the apical end.

A number of other experiments that I made, in which pieces of
antennularia were fixed to a rotating wheel, gave negative results,
since neither roots nor stems appeared on the pieces. The rubbing
of the ends of the piece against the water as the wheel turned round,
or else the agitation of the water, prevented, most probably, the
regeneration from taking place.

How gravity acts on antennularia has not as yet been determined.
The only suggestion that we can offer at present is that it brings
about a rearrangement of the lighter and heavier parts of the tissues.
A rearrangement of this sort has been demonstrated when the egg of
the frog is inverted, and in consequence certain changes are brought
about in the development that will be described in another chapter.

### EFFECT OF CONTACT

The contact of a newly forming part with a solid body has been
shown by Loeb in a few cases, at least, to be a factor in regeneration.
If a piece is cut from the stem of the tubularian hydroid *Tubularia*

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*mesembryanthemum*, and the piece held so that its basal end comes in contact with a solid body, a root develops at that end. If a piece is held in a similar position, but with its apical end in contact with a solid body, a root does not develop from this end. Evidently the development of a root in this form is also connected with an internal factor; but that there is in reality a reaction in this case, and not simply the development of a root at the basal end, is shown by the follow-
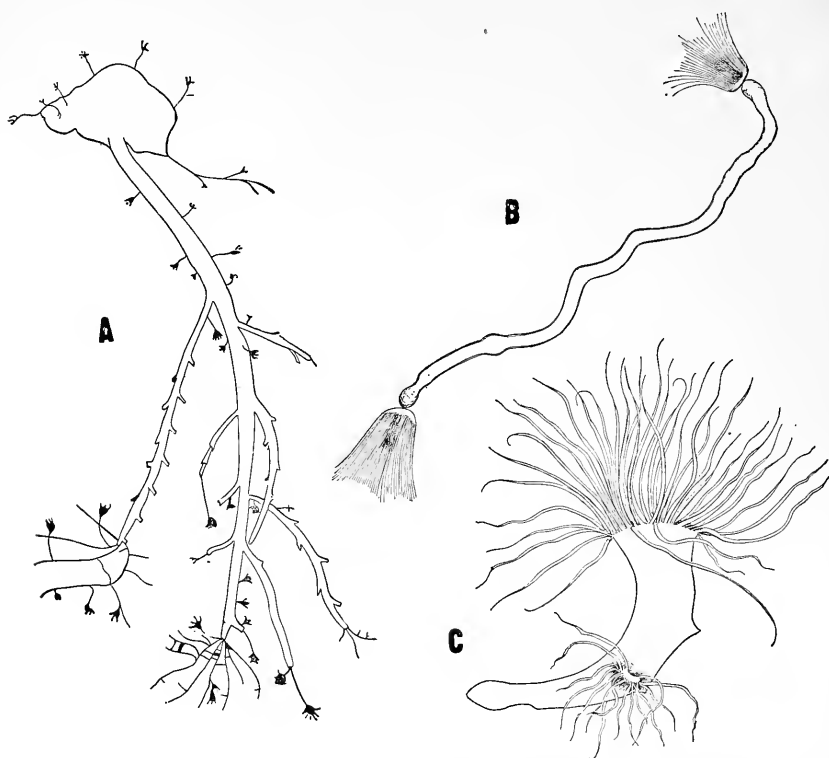


FIG. 15. — After Loeb. *A*. A piece of the stem of margelis placed in a dish. Roots come off where stem touches dish, and polyps at other points. *B*. Piece of the stem of tubularia producing a hydranth at each end. *C*. *Cerianthus membranaceus*. Piece cut from side producing tentacles only on oral side of cut.

ing experiment: If a piece is cut from the stem and suspended so that both ends are surrounded by water — it makes no difference whether the piece is vertical or horizontal — a hydranth develops first on the apical end, and then another on the basal end (Fig. 15, *B*). When the apical end of a piece is stuck in the sand, leaving the basal end free, a hydranth develops on the latter, but not on the end in the sand.

In another hydroid, *Margelis carolinensis*, studied by Loeb, the effect of contact is more easily demonstrated. If a branch of margelis

is put into a dish of water and is kept from all motion, the parts that come in contact with the dish produce roots that attach themselves. Even the apical end of the stem may grow out as a root, as shown in Fig. 15, *A*. Those parts of the branch that are not in contact with any solid object give rise to new hydranths. Another hydroid, *Pennaria tiarella*, also shows, according to Loeb, the same response to contact. In this connection it is interesting to find that a growing hydranth of pennaria, if brought in contact with a solid body, turns away from the region of contact and bends at right angles to the body which it touches. We find, once more, that a factor having an influence on the growth of the animal has also a similar influence on the regeneration.

Loeb has found that if pieces of the hydroid *Campanularia* are cut off and placed in a dish filled with sea water, all the hydranths that touch the bottom of the dish are absorbed and transformed into the substance of the stem. The cœnosarc may creep out of the stem wherever it comes in contact with the glass, and produce stolons that give rise to new polyps on their upper surfaces. Loeb shows that growth takes place at the end of the stolon that pushes out of the perisarc, and this growing region draws the rest of the cœnosarc after it. If a new hydranth appears along the old piece, the cœnosarc is drawn towards the hydranth.

### EFFECT OF CHEMICAL CHANGES IN THE ENVIRONMENT

Temperature, light, gravity, and contact are the most familiar kinds of external physical agencies that have a direct influence upon the growth of organisms. Food, though coming from the outside, yet acts only after it has entered the body. Organisms that live in water may be affected by the quantity and the kinds of the salts contained in the water, and also by the dissolved gases. The only experiments that have been made to show the influence of this last class of agents on animals are those made by Loeb. He placed pieces of the stem of tubularia in sea water of different degrees of concentration. After eight days the pieces, that had meanwhile produced hydranths, were measured. It was found that the maximum growth in length takes place, not in normal sea water, but in a much diluted solution. Loeb interprets this result to mean that the cells of tubularia must have a certain amount of turgidity in order to grow, and this is possible so long as the concentration does not pass a certain limit. This limit is reached by the addition of 1.6 grams of sodium chloride to each 100 c.c. of sea water. With a decrease in the concentration, the cells become more turgid, the maximum point corresponding to the maximum amount of growth. Below this point the solution is sup-

posed to act as a poison. The most important result of this experiment is to show that the maximum growth does not take place in sea water in which the animal is accustomed to live, but in a much more dilute solution. Normal sea water contains about 3.8 per cent of salts; the maximum growth takes place in a solution containing only 2.2 per cent. Not only is the length of the stem greater in the latter solution, but the thickness of the stem is also greater. The stem is smaller in a solution containing more salt than that contained in ordinary sea water.

There is another variant in these solutions which Loeb takes into account. With the increase in concentration of the solution its power of absorbing oxygen decreases, but the difference is too slight to affect the main result.

Not only does the amount of salts in solution affect the osmotic condition of the cells, but the salts also play a part in the metabolism of the animal. As the result of a series of experiments, the details of which may be here omitted, Loeb has shown that the regeneration of tubularia takes place only when the salts of potassium and of magnesium are present. A very little of the potassium salt is necessary, too much retards, and still more prevents regeneration.

There must be also a certain amount of oxygen dissolved in sea water in order that regeneration may take place. If a piece of the stem of tubularia is cut off and one end pushed into a small tube that fits the stem closely, and if the tube is then stuck into the sand at the bottom of an aquarium, a hydranth develops only at the free end of the piece, and none at the end in the tube. The result appears to be due to the lack of oxygen. If the piece is then taken from the tube, a hydranth may appear at the end that has been in the tube.

Another experiment shows the same result even more clearly. If a piece of the stem is suspended freely in the water, so that its lower end is almost in contact with the surface of the sand, but does not quite touch it, no regeneration takes place at the lower end. This result is interpreted by Loeb as due to the lack of oxygen in the water near the surface of the sand.[1]

### GENERAL CONSIDERATIONS

In connection with the action of external factors on regeneration it is evident that in some cases they may not be in themselves necessary for the growth of a new part, yet when growth takes place they may determine what sort of a part is produced. For instance, if gravity

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[1] Jacobson has shown that the layer of water just above the sedimentary layer at the bottom is poor in oxygen.

determines the kind of regeneration in antennularia, it is possible that if the regenerating piece were placed on a rotating wheel, the piece might still produce a new stem at the apical end, and roots at the lower end.    In an experiment of this sort that I made, the pieces did not, it is true, regenerate at all, but this was probably due not to the change of position in regard to gravity, but to agitation of the water, or to the rubbing of the cut-end against the water.    It is also possible that in this form the attachment of the piece at one end may be a factor that may counterbalance the action of gravity.    Other factors, such as food, or temperature, or oxygen, appear not to determine the kind of product that results, but only the rapidity with which the change takes place.    The salts in solution seem also to act on the rate and extent of the new growth, but possibly other cases may be found in which the kind of regeneration may also be affected by the salts.

It is important to find that those animals whose growth and regeneration are influenced by such external factors as light, gravity, and contact are attached animals that stand in a constant relation to these physical agents.    They form only a very small part of the entire number of animals in which regeneration takes place.    Animals that constantly move about are not, as a rule, influenced during their growth and regeneration by gravity and contact, and under natural circumstances they are always changing their position in regard to these agents.    Temperature, and food, and substances in solution act alike on fixed and free forms, and they are, it appears, both influenced in the same way by these agents.    The most signifi-cant fact that has been discovered in connection with the influence of external factors on regeneration is that the same factors that influ-ence the normal growth of the organism also affect in the same way the regeneration.

As yet an analysis of the external factors that influence growth has not been made out as completely for animals as for plants, especially in those cases in which the result is determined by several factors at the same time.    An examination of the factors that influence regeneration in plants will be made in a later chapter.    First, how-ever, the internal factors of regeneration in animals will be consid-ered.

# CHAPTER III

## THE INTERNAL FACTORS OF REGENERATION IN ANIMALS

THE comparatively few cases in animals in which regeneration has been shown to be influenced by external factors have been given in the preceding chapter. In all other cases that are known the factors are internal. By this is meant that we cannot trace any direct connection between the result and any of the known external agents that have been shown in other cases to have an influence on regeneration. Certain external conditions must, of course, be present, such as a supply of oxygen, a certain temperature, moisture in some cases, etc., in order that the process may go on, but they are without influence on the kind of regeneration, and are necessary for all parts alike.

### POLARITY AND HETEROMORPHOSIS

Trembley, Spallanzani, and Bonnet knew that, in general, at the end of a piece of an animal from which a head has been cut off a new head develops, and from the posterior cut-surface of a piece a new posterior part is regenerated. Allman was the first to give the name "polarity" to this phenomenon.[1]

In several animals regeneration takes place more readily from one end than from the other of the same cut, and this difference seems to be connected with the kind of new part that is to be regenerated, and not with the actual power of regeneration of the region itself. For instance, if a short piece is cut from the anterior end of an earthworm, a new anterior end is quickly regenerated from the anterior cut-surface of the posterior piece, but no regeneration takes place, or only after a long time, from the posterior cut-surface of the anterior piece. These relations are reversed if the posterior end of a worm is cut off. There regenerates very quickly a new posterior end from the posterior cut-surface of the anterior piece, but no regeneration takes place, or only after a long time, from the anterior cut-surface of the posterior piece. The new structures that develop after a long time from the posterior surface of a short anterior piece, and from

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[1] "There is thus *manifested in the formative force of the tubularia-stem a well-marked polarity*, which is rendered very apparent if a segment be cut out from the centre of the stem." Allman ('64).

the anterior surface of a short posterior piece, correspond to a different part of the worm from that which would be expected to develop, if the polarity of the piece is taken into account.   Another reversed head develops on the posterior cut-surface of the anterior piece, and
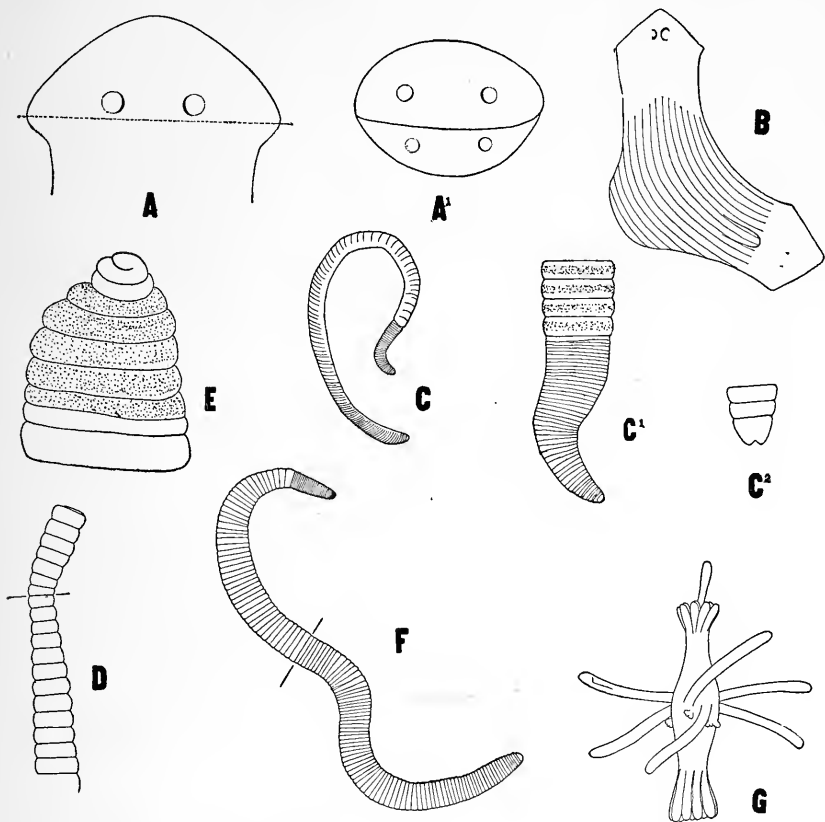


FIG. 16.—*A.* Head of *Planaria lugubris* with line indicating level at which *A¹* was cut off. *A¹.* Head of last regenerating a new head at its posterior end.   *B.* Piece of *P. maculata* regenerating head at each end.   *C.* Posterior end of *Allolobophora fœtida* regenerating a new tail at its anterior end.   *C¹.* Enlarged anterior end of last with new tail.   *C².* Tip of new tail. *D.* Anterior end of one individual of *A. fœtida*, grafted to anterior end of another worm, leaving posterior end of piece exposed.  This has begun to regenerate.   *E.* After Hazen. Similar experiment in which *a new head* regenerated at posterior end of grafted piece. *F.* Two longer pieces of *A. fœtida* united by anterior ends.   One end was subsequently cut off and a new tail regenerated.   *G.* End of a developing piece of *Tubularia mesembryanthemum* that had been cut off; it has regenerated, at its proximal end, another proboscis.

another tail on the anterior end of the posterior piece.   The polarity of the new part is in this case reversed, as compared with that of the piece from which it arises.   In the earthworm there is a marked delay in the regeneration of these heteromorphic parts.   Even in tubularia in which heteromorphosis takes place, there is usually a

delay of twenty-four hours in the formation of the reversed head. In *Planaria lugubris*, in which a reversed head develops, if a piece is cut from the anterior end just behind the eyes, the delay in the formation of the reversed head is very slight, if indeed there is any delay at all.

In the earthworm and in the planarian the production of reversed structures appears to be connected with the part of the body through which the cut is made, and to be due to internal factors. The question arises whether the presence of certain organs at the exposed surface can account for the result. It is conceivable that if such organs are present, and produce new cells that go into the new part, the presence of such cells may be the factor that determines what the new part will become; and in consequence the polarity of the part may be reversed. For example, the presence of the cut-end of the œsophagus or of the pharynx at the posterior surface of the anterior piece of the earthworm may determine that a new pharynx develops at the cut-end, and this may in turn act on the rest of the new tissues in such a way that a head rather than a tail is formed. When a posterior piece is cut off, the presence of the stomach-intestine at the cut-end may influence the new part, so that a tail is produced. It can be shown, however, that a new head may arise at the anterior end of a piece that contains only the stomach-intestine, as sometimes occurs when the worm is cut in two anterior to the middle; and it is not improbable that a tail can be produced from the posterior end of a piece that contains the old œsophagus, and perhaps even the old pharynx. In the planarian I have especially examined this point, but I have not yet found that the result can be referred to the cut-surface passing through any particular organ, or to the absence of any organs at the cut-end.

If, instead of referring the result to any one organ, we assume that the tissues near the cut-ends are specialized in such a way that they can only produce their like, and that the sum total of tissues of this sort making up the new part determines the result, we can only suggest that this may be so, but we cannot show at present that it is so, or that the result could be brought about in this way.

We might make an appeal to the hypothesis of formative stuffs, and assume that there are certain substances present in the head, and others in the tail, of such a sort that they determine the kind of differentiation of the new part; but this view meets also with serious objections. In the first place, it gives only the appearance of an explanation because it assumes both that such stuffs are present, and that they can produce the kind of result that is to be explained. Until such substances have been found and until it can be shown that this kind of action is possible, the stuff-hypothesis adds nothing to

the facts themselves, and may withdraw attention from the real solution of the problem.

Bonnet, who first proposed the hypothesis of specific stuffs, went further and assumed also that they move in definite directions in the body, the head-stuff flowing forward and the tail-stuff flowing backward. It was necessary to assume definite movements of the stuffs in order to account for the development of the head at the anterior end of a piece and of a tail at the posterior end. In cases of heteromorphosis of the sort described above, these stuffs, if they brought about the results, would have to move in *opposite* directions from those assumed in the hypothesis ; or else that part of the hypothesis that postulates the movement of the substances must be dropped, and in its place there must be substituted the idea of the excessive amount of such substances in the ends accounting for the heteromorphosis. An hypothesis that must be changed in this fundamental way to explain both classes of facts cannot be given very serious consideration. Of these possible ways in which it has been attempted to account for the phenomenon of heteromorphosis, the first one suggested seems to me simpler and more probable, but which organs are to be made responsible for the result cannot at present be stated. The fact that both Bardeen and I have obtained heteromorphosis in planarians in other regions than in the head indicates at least that other factors than the presence of head tissues or of head substances may bring about the development, and if it can be discovered what produces the result in regions remote from the head we may be in a position to explain the result in the head region in the same way, although it may be, of course, that the same result may be brought about by different factors, when the internal conditions are somewhat different.

Another phenomenon connected with the polarity of a piece is shown by *Cerianthus membranaceous*. When a triangular piece is cut from the side of the body, a half circle of tentacles appears around the lower edge of the cut, as shown in Fig. 15, *C*. The presence of a free distal edge on the lower side of the opening is a sufficient stimulus to call forth the development of tentacles.
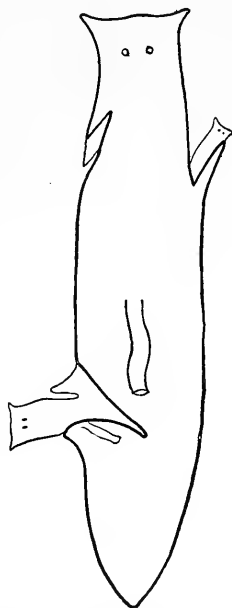


FIG. 17. — After Voigt. Planarian with three oblique cuts at side. The most anterior cut (left side), directed forward, produced a tail. The one on the right side, directed backwards, produced a head. The most posterior cut (left side) made a head with pharynx, and also a tail-like outgrowth.

A somewhat similar result is obtained when an incision is made in the side of the body of a planarian. A lateral head may grow out from the anterior edge of the cut-surface, as shown in Fig. 17.

It has been shown by Loeb that if the incurrent siphon of the ascidian *Ciona intestinalis* be partially cut off, new eye-specks develop around the margin of the cut, as shown in Fig. 18, *A*. I have repeated
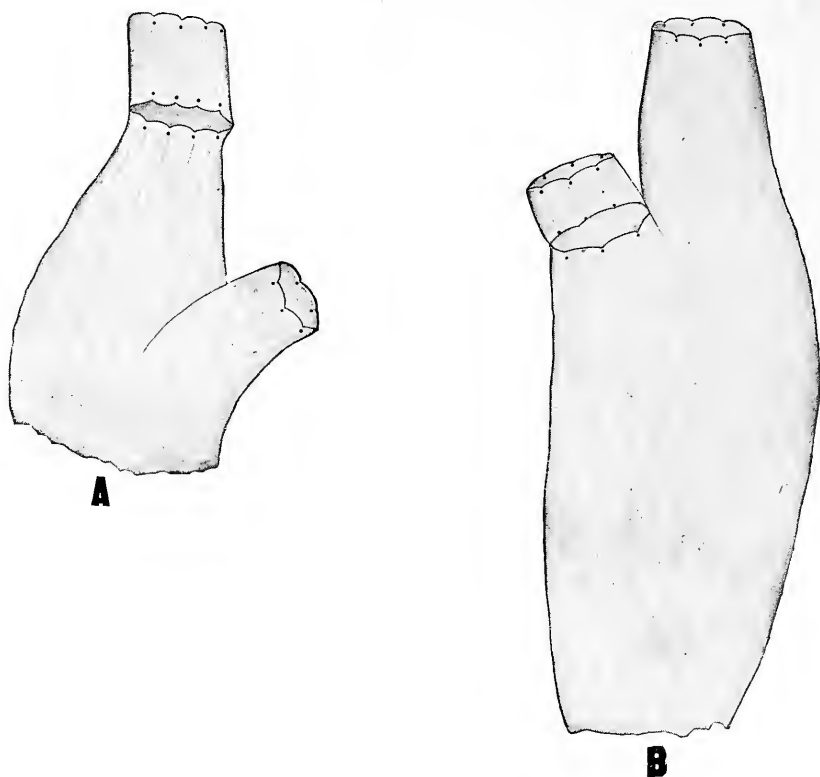


FIG. 18. — *A*. After Loeb. Anterior end of *Ciona intestinalis* with oral-siphon partially cut off. Eye-specks regenerate, both on oral and aboral edge. *B*. Same (after T. H. M.), showing similar result on excurrent siphon.

this experiment and obtained the same result, and found, as had Loeb also, that the same holds true for the excurrent siphon (Fig. 18, *B*). In these cases the new eyes appear both on the anterior and posterior edges of the cut. Most probably the result is connected with an external stimulus, rather than with an internal one. This may be true also for cerianthus, but probably not for the planarian.

## LATERAL REGENERATION

Since the most familiar cases of regeneration are those that take place at the anterior and posterior ends, we not unnaturally come to think of polarity as a phenomenon connected only with the long axis of the animal; but there are also many cases of lateral regeneration in which a similar relation can be shown. In such a case as the regeneration of the leg of a salamander, or of a crab, we find instances of lateral regeneration, but since the development takes place in the direction of the long axis of the leg, the polarity of the leg may be thought of as substituted for that of the body. In other animals, however, the regeneration is strictly lateral. I have found that if the anterior end of an earthworm, or even of lumbriculus, is split lengthwise in halves, and then one of the half-pieces is removed, the missing half is replaced by the half left attached to the rest of the worm. Trembley split a hydra lengthwise into two pieces, and each piece bent inwards to make a new tubular body. Bickford, Driesch, and I have obtained similar results with pieces of the stem of tubularia.

In planarians which have a flat, broad body, lateral regeneration takes place readily. If a worm is split in two along the middle line of the body (Fig. $13\frac{1}{2}$, *A*), each half regenerates the missing half. This is brought about by the development of new tissue along the cut-side, and the extension into the new part of outgrowths from the digestive tract. Lateral regeneration also takes place if the worm is split lengthwise into two unequal parts. In this case the larger piece produces new material along the cut-side, and into this new part the branches of the old digestive tract extend. The smaller piece also produces new material along the cut-side, a new pharynx appears along the line between the old and the new tissue, and a new digestive tract is formed out of the remains of the old one (Fig. 19, *a*, *b*, *c*). New branches grow out of the fused part into the new tissues at the side. The new worm that develops from a piece that is less than half the width of the old worm is about as wide as the piece that was cut off, for what is gained at the cut-side is lost in the old part. The piece loses in length also during regeneration. If the new worm is fed, it increases in size, gaining in breadth both on the old side, as well as on the new side, and in time it becomes a full-grown, symmetrical worm.

In the formation of the new part in these cases of lateral regeneration it is not difficult to understand how some of the old organs, as the digestive tract, grow out laterally into the new part; but it is more difficult to see how longitudinal organs, such as the nerve-cord and genital ducts, are formed anew. Bardeen, who has examined the

development of the new nerve-cord in lateral pieces, thinks that the new nerve-cord grows backwards in the new part from the brain that develops at the anterior end, either out of the old brain, if it, or any part of it, is left, or out of the new brain that develops from the anterior end of the lateral cord that is present in the piece. What takes place in pieces cut so far to one side that none of the old cord is present in the piece he did not make out; but I can state that a new brain develops even when none of the lateral cord is present.
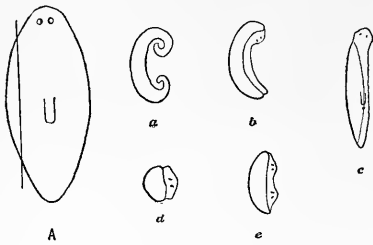


FIG. 19. — Indicating how a piece is cut off from side of *Planaria maculata*. *a, b, c*. Regeneration of last. *d*. Regeneration of single head at side. *e*. Regeneration of two heads at side.

The development of a new head in pieces cut to one side of the old median line offers some facts of interest. A piece may be cut from the side of a planarian of such a shape that it has no anterior surface at all (Fig. 19, *A*); yet a head develops at the anterior end of the new material that appears at the side. It stands at first to one side, later it assumes an anterior position. In this case an axial structure arises in a lateral position, unless we look upon the new head as arising at the anterior end of the new part, rather than at the side of the old, but there is no evidence in favor of such an interpretation, since the head arises at the same time as does the rest of the new material at the side. In a small piece all of the new material at the side may be used to form the new head (Fig. 19, *d*). Sometimes two heads develop (Fig. 19, *e*).

### REGENERATION FROM AN OBLIQUE SURFACE

There are also certain important facts connected with the regeneration from an oblique surface. The first case of the sort was described by Barfurth. He found that if the tail of a tadpole is cut off obliquely, as shown in Fig. 20, *B*, the new tail that develops stands at first at right angles to the oblique surface. The angle that the new tail makes with the axis of the old tail will be in proportion to the obliquity of the cut-surface. The notochord that occupies the centre of the new tail begins at the end of the old notochord, and extends to the tip of the new tail, dividing it in the same proportionate parts as does the notochord of the normal tail. The other organs occupy corresponding positions. As the new tail becomes larger it slowly swings around into line with the old part. This phenomenon of regeneration from an oblique surface has been found in a number of other forms. It has been described by Hescheler, and by myself

in earthworms (Fig. 20, $D$), both for the anterior and posterior ends. I have shown that it also takes place in the tail of a teleostian fish, fundulus (Fig. 20, $C$), and have offered the following explanation of the phenomenon. The new material that is first laid down is, to a certain extent, indifferent as regards its axes. A symmetrical struc-
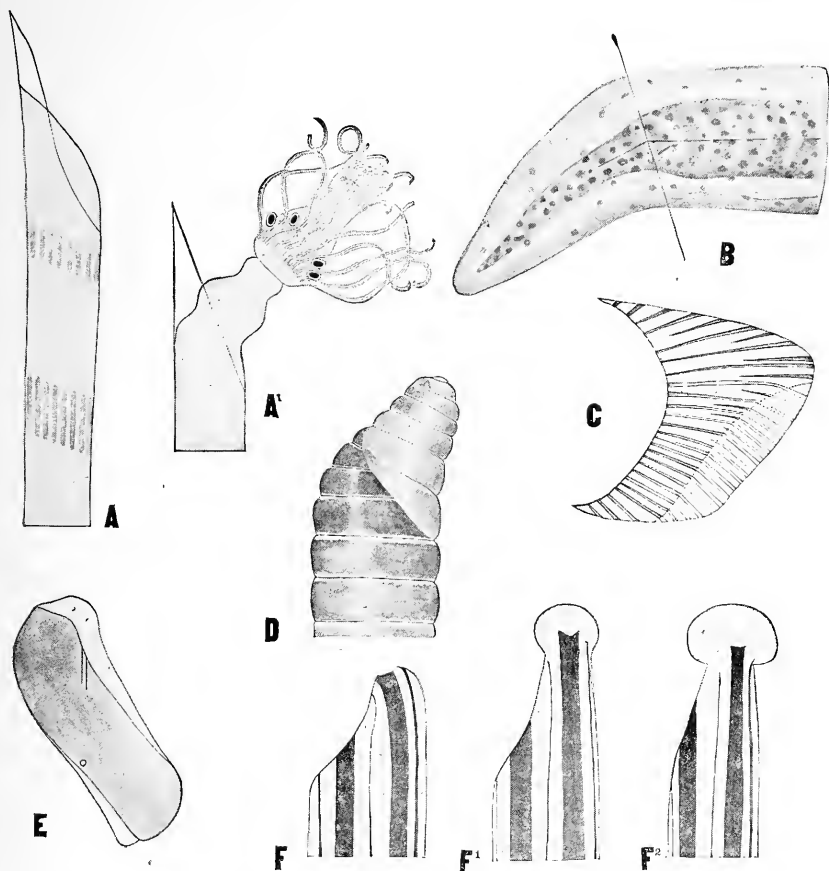


Fig. 20. — $A$, $A^1$. After Driesch. $A$. Piece of stem of tubularia cut off obliquely, showing oblique position of tentacles. $A^1$. Same, later stage. $B$. After Barfurth. Tail of tadpole regenerating from oblique surface. $C$. Tail of fundulus regenerating from oblique surface. $D$. After Hescheler. Anterior end of allolobophora regenerating from oblique surface. $E$. Piece of planaria, cut off by two oblique cuts, regenerating new head and tail. $F$, $F^1$, $F^2$. Three stages in the development of a new head (of a piece of bipalium) at anterior end of oblique surface.

ture is then formed, with the old edge as a basis. The median point of the cut-edge connected with the median point of the outer surface of the new edge, gives the axis of symmetry of the new tail. The other regions assume corresponding positions. In the tail of the tadpole the position of the new notochord is determined by the

cut-end of the old notochord and the median, outer point of the new material, and since the new material is at first equally developed along the cut-edge, or at least symmetrically developed, the new tail must stand at right angles to the cut-edge. This explanation will cover, I think, all cases of regeneration from an oblique surface. It assumes a law of symmetry in the new material that is in accordance with the observed position in which the new structure appears. The hypothesis makes no pretence to explain why the new structures *should* assume a symmetrical position, but given that they do, the observed result follows.

There are certain peculiarities connected with the regeneration from an oblique surface in planarians that may be considered in this connection. If the worm is cut in two by means of an oblique cut, as shown by the oblique line in Fig. 21, *B*, the new head that appears
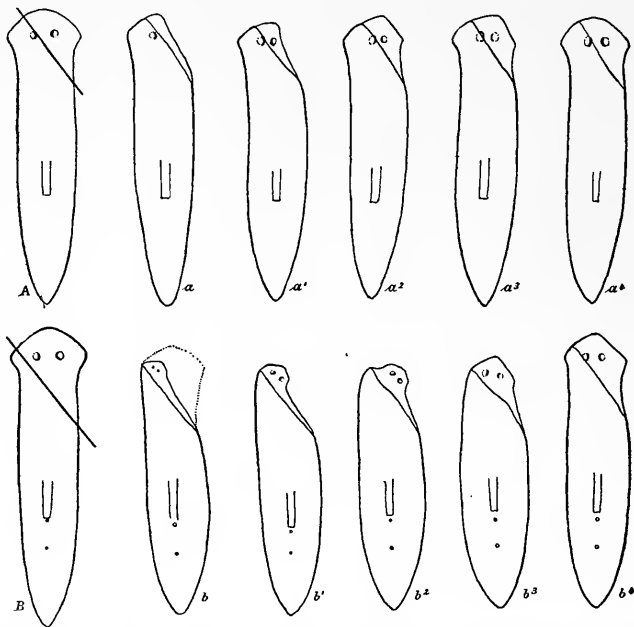


FIG. 21. — *Planaria lugubris.* Upper row. *A.* Part of head cut off obliquely; *a–a⁴*. Regeneration of new head. Lower row. *B.* More of head cut off obliquely; *b–b⁴*. Regeneration of same.

on the anterior cut-surface of the posterior piece appears *at one side* and not in the middle of the oblique surface (Fig. 21, *B*, *b*). The new head stands at right angles to the cut-surface. The anterior piece of the worm produces a new tail at the side of the posterior cut-surface, in the same way that the tail is formed in Fig. 20, *E*. The tail also stands at right angles to the cut-surface. The new pharynx

that develops in a piece of this kind appears in the middle of the posterior cut-surface, between the old and the new parts.    It may extend somewhat obliquely in the new part, and point toward the new tail.

If a piece is cut from the anterior part of a worm by two oblique and parallel cuts, the new head appears at one side of the anterior cut-surface, and the new tail at the other side of the posterior cut-surface.    The new pharynx appears in the new material of the posterior part in the middle line.    Thus the middle lines of the new head and tail and pharynx lie in different positions, yet these parts are
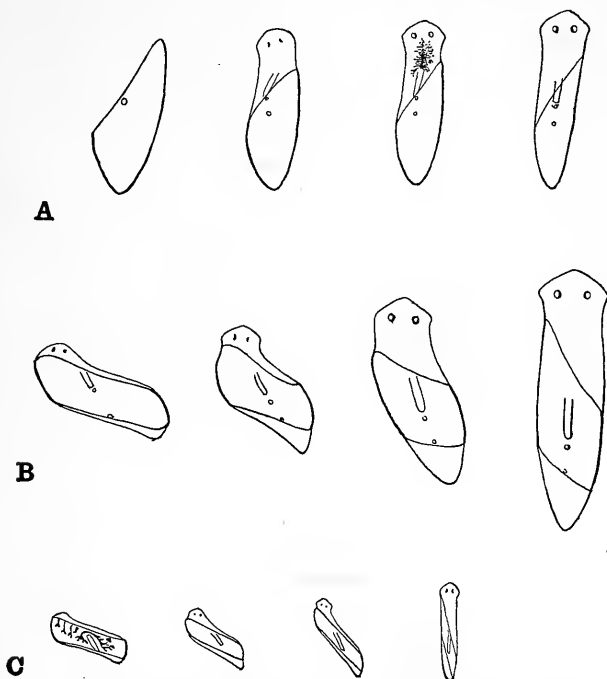


FIG. 22. — Two upper rows *Planaria lugubris.* Lower row *Planaria maculata.* Upper row. Tail-piece cut off obliquely in front of genital pore. Figures show mode of regeneration. Middle row.  Piece including old pharynx cut off by two cross-cuts, regenerating head and tail.   Lower row.   Piece cut off as last, regenerating head and tail.

subsequently brought into the same line.    This is done by the head extending more forward and becoming broader, the tail growing backward and also becoming broader.    The old piece becomes narrower at the same time.    These three changes going on simultaneously produce a new symmetrical worm.    In one form, *Planaria lugubris,* the symmetrical form is reached largely by the forward growth and the enlargement of the head, and the growth backward and the enlargement of the tail (Fig. 22, *B*).    In *Planaria maculata* the old part shifts, so that it forms a new median line connecting the median line of the new head

and new tail. This is best shown when the piece includes the old pharynx (Fig. 22, *C*). The pharynx is also shifted, so that its anterior end points towards the side at which the new head lies, and its posterior end towards the new tail. The result is that a new symmetrical worm is formed, as shown by the series of figures in Fig. 22, *C*. In *Planaria maculata* the changes take place largely in the old part, and the old material extends throughout the entire length of the new worm. In *Planaria lugubris* the change takes place largely in the new parts (Fig. 22, *B*). The general method in the latter species by which the symmetry is attained can be best shown by cutting the worm in two by an oblique cut just in front of the genital pore (Fig. 22, *A*). The posterior piece produces a new head at the side, and a new pharynx appears along the border between the new and the old parts, as shown in these figures. Its posterior end touches the middle line of the old part, and from this point it extends obliquely across the new tissue towards the middle of the new head. As regeneration goes on the new head is carried farther forward, it becomes larger, and the main region of new growth is found to be, in the figure, to the left side of the new part. As a result of these changes the new head turns forward, and comes to lie nearer the middle line of the old part. The pharynx is also turned more forward, and finally, as the new parts enlarge, the symmetrical form is produced. The internal factors that are involved in the development of these oblique pieces are very difficult to analyze. The position of the new head and tail at one side of the cut-edge is the most difficult phenomenon of all to explain. We may, I think, safely regard the first new material that is proliferated along the cut-edge as totipotent, and our special problem resolves itself into discovering what factor or factors determine that the new head is to form at the most anterior end of the new material, and the new tail at the most posterior end. If we assume that the result is in some way connected with the influence of the old part on the new, and that this influence is of such a sort that the more anterior part of the old tissue determines that one side of the head must be at the most anterior edge, we have at least a formal explanation of the position of the head at the side. Given the position of the new head fixed at one side, its breadth will be determined by the maximum breadth possible for the formation of a new head. This is also in part an assumption, but it has at least certain general facts of observation in its favor. The oblique position of the new head is the result of its symmetrical development in the new material in the same way that the position of the tail of the fish or of the tadpole is the result of the symmetrical formation of the new tail on the oblique surface. The subsequent changes, by means of which a symmetrical worm is developed, are the result of different rates of growth

in the different parts.   In this connection the most important fact is that the growth takes place most rapidly where it will bring about the new form.   This problem, which is one of the most fundamental in connection with the phenomena of development and of regeneration, will be more fully discussed in a later chapter.

A number of assumptions have been made in the above attempt to give an analysis of the formation of a head at the side of an oblique surface.   That these assumptions are not entirely arbitrary, but have a certain amount of evidence in their favor, can, I think, be shown. The new material that first appears is supposed to be totipotent, in the sense that any part of it may produce any part of the structure that develops from this material.   That this is probable is shown by the following experiment.   If a cross-piece is cut from a worm, and then split lengthwise into halves, each half will produce a new head at the anterior edge of the piece.   This result shows, at least, that from the tissue lying to the right or to the left of the middle line new material may be formed from which a whole head may develop.   The new head does not stand at first with its middle axis in line with the middle of the old piece, *i.e.* it does not stand squarely at the anterior end of the half-piece, but more towards the inner side of the piece. It may appear that the old part has sufficient influence on the new part to shift the axis of the latter toward the old middle line, but while some such influence may be present, it is probable that the position of the head is in part the outcome of another factor, viz. the presence at the inner side of the piece of an undeveloped new side, with which the explanation of the less development of the inner side of the head is also connected.

If a cross-piece is cut from a worm and kept until a small amount of new tissue appears over the anterior and posterior cut-surfaces, and if then the piece is split in two lengthwise, there will develop from each piece a new head out of the new material over the anterior surface.   The result shows that the new material is at first totipotent, in the sense that it may still produce one or more heads according to the conditions.   It is possible, of course, that the formation of the new



FIG. 23. — *Planaria maculata.   A.* Cross-piece, allowed to regenerate, then cut in two lengthwise, as indicated by line.   *a–a⁵*. Regeneration of left half.

head may have begun at the time of the experiment, but if it had, the development had not gone so far that a new arrangement was impossible.   If, however, the piece is not cut lengthwise until just before the formation of a head (Fig. 23, *A*), then each half-piece produces at first a half-head, that completes itself later at the cut-side.

E

Another experiment shows even more satisfactorily that the material over an anterior cut-edge may produce one or more new heads according to the conditions, and that the result is not connected with the region from which the new material is derived. If the anterior end of a planarian is cut off and then an oblong piece is removed from the middle of the worm, as shown in Fig. 24, *A*, it will be found, if
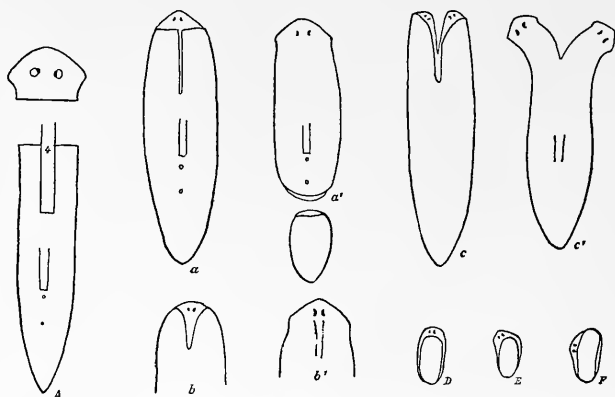


Fig. 24.—*Planaria lugubris.* *A.* Showing where a piece, 4, was removed from middle of a worm. *a, b.* Regeneration of a single head. *c, c¹.* Regeneration of two heads. *D, E, F.* Regeneration of small piece, 4, that was cut out.

the side parts are kept from fusing together in the middle line, that a new head develops at the anterior end of each part, as shown in Fig. 24, *c, c¹*. If, on the other hand, the two sides come together and fuse in the middle line, as shown in Fig. 24, *a, b,* the new material that appears over their anterior ends becomes continuous and produces a single head. In this case, although the middle part of the old tissue has been removed, a single head develops that is normal in all respects, and the eyes are not nearer together than when the middle part is present, as when regeneration takes place from an anterior cross-cut surface.

The assumption that the lateral position of the head on an oblique surface is connected with the more anterior region of the old material that is found at that side, can be made at least more intelligible by the following experiment: If the head of a planarian is cut off obliquely, as indicated in Fig. 21, *B,* so that one of the "ears" is left at one side, the new head arises at the side in connection with the part of the old head that lies at that side. The new head does not extend over the entire cut-surface, which is longer of course than a cross-cut would be, but lies at one side, as in the other cases just described. In this case we can see that if the new head cannot, on account of certain conditions, extend over the entire cut-surface, one side of it may be determined by the presence of a part of the old head,

and this influence may be stronger than any other that might tend to locate the new head in the original middle line. If we suppose that similar conditions prevail in all cases when oblique surfaces are present in these worms, we have a formal solution of the problem. The argument cannot be convincing unless we can give a further explanation of the nature of this influence that the old part has upon the new.

In other cases, as in the regeneration from an oblique surface in the tail of the tadpole and of a fish, we must assume that the factor that determines the middle of the new part has a stronger influence on the new material than has the most posterior part of the old tissue.

The influence of an oblique cut-surface on the position of the new parts is shown in a different way in the hydroid, tubularia. The conditions are different in this case inasmuch as there is no proliferation from the cut-end, but the old part produces the new hydranth. Driesch found that if the stem of tubularia is cut in two obliquely, the new tentacles, that develop as two rings around the tube near its cut-end, stand obliquely on the stem,[1] as shown in Fig. 20, *A*. In most cases, both the distal and the proximal circles of tentacles lie obliquely to the long axis of the stem, but there is some variability in the result, and occasionally one or the other, especially the proximal circle, may be squarely placed, although, as a rule, the influence of the oblique cut-end can be seen. It can be shown, I think, that the oblique position of the rings of tentacles in tubularia is the outcome of factors different from those that are found in the regeneration of the tail of the tadpole and of the head and tail of the planarian. Driesch suggested that the distance of the tentacle-rings from the cut-end is the result of some sort of " regulation " that determines their position at a given distance from the region at which the surrounding water acts on the exposed end. Hence, if the exposed surface is an oblique one the rings will also be formed in an oblique position. On the other hand, I have suggested that we can imagine the regulation to result from other factors. At the beginning of the development, and before the tentacles appear, there is a withdrawal of tissue from the cut-end that leaves the region from which the proboscis develops quite thin. If this material withdraws at a uniform rate and to the same distance at all points from the end of the piece, as observation shows to be the case, and if, as appears also to be true, the outer end of the distal ring of tentacles lies at the inner end of the proboscis region, then it too will assume an oblique position if the cut-end is oblique. If we imagine a similar series of regulations taking place throughout

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[1] The same holds good for the basal hydranth if it arises near an oblique end.
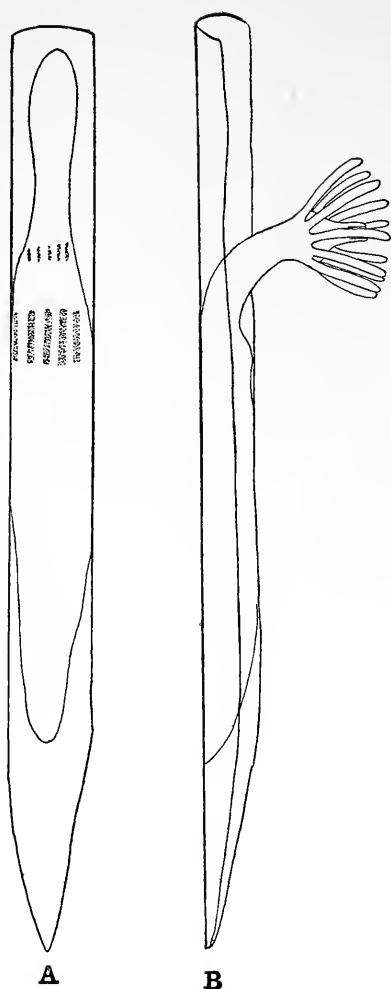
FIG. 25. — Piece of stem of *Tubularia mesembry-anthemum* split in two lengthwise. Formation of whole hydranth that turned away from contact with old perisarc.

the piece, we can account for the results. On this hypothesis the action of the water on the free end need not be a factor in the result, but the oblique end is itself sufficient to determine the series of regulations, or mass-relations, that lead to the laying down of an oblique hydranth.

When the hydranth protrudes from the stem it assumes an oblique position, as shown in Fig. 20, $A^1$. Driesch supposed the oblique position of the hydranth to be due to an oblique zone that develops behind the hydranth, but the result can best be explained, as certain other experiments that I have made seem to show, as due to the negative thigmotropism of the hydranth at the time it protrudes from the old perisarc. It turns away from the projecting side of the oblique end of the perisarc, as it does from any solid body with which it comes in contact. That this is the case is best shown by splitting the stem lengthwise into halves. In this case, although the two circles of tentacles may be laid down squarely (Fig. 25, $A$), the new hydranth protrudes at right angles to the old perisarc, as shown in Fig. 25, $B$.

## THE INFLUENCE OF INTERNAL ORGANS AT THE CUT-SURFACE ON THE NEW STRUCTURE

In a few cases it has been discovered that the presence of certain organs at the exposed surface is necessary in order that regeneration may take place. The following experiment that I have recently carried out shows, for instance, the influence of the nerve-cord on the regenerating part. A few of the anterior segments of the earth-

worm are cut off, as shown in the left-hand figure in Fig. 26, and then a piece of the mid-ventral body wall of the worm is cut out, a part of the ventral nerve-cord being removed with the piece. The cut-edges meet along the mid-ventral line and fuse, closing the wound. As a result of the operation there is left exposed, at the anterior end of the worm, a cut-surface with all of the internal organs present except the nervous system. The anterior end heals over, but I have not observed the development of a new head at this level, although the exposed end is in a region at which, under ordinary circumstances, a new head readily regenerates. In several cases a new head developed at the point where the cut-end of the nervous system is situated, *i.e.* at the level *B* in the figure.

A variation of the same experiment shows still more conclusively the importance of the nervous system for the result. A few anterior segments are cut from the anterior end as before. A cut is made, as shown in the right-hand figure in Fig. 26, to one side of the mid-ventral line (indicated by the black line in the figure at the level *A*). Then, at the posterior end of this cut a piece is removed from the mid-ventral line as in the former experiment (shown by the stippled area in the figure). A portion of the ventral nerve-cord is removed with the piece. As a result of this operation, two anterior ends of the nervous system are left exposed (shown by the black dots in the figure). At the anterior end of the worm, *i.e.* at *A*, there is one exposure, and at the posterior end of the region from which the piece was removed there is another. Two heads develop in successful



FIG. 26. — Left-hand figure *X* shows how, after cutting off the anterior end of *Allolobophora fœtida*, a piece of the ventral wall (including a part of the nerve-cord) is cut out. Right-hand figure *Y* illustrates a more complicated operation, in which the piece of the ventral wall that is cut out is a little behind the anterior end.

cases, one at the anterior end of the anterior cut-surface, *i.e.* at *A*, and the other at *B*.

The results show that in the absence of the cut-end of the nervous system at an exposed surface a new head does not develop; and conversely, the development of a new head takes place when the anterior

end of the nervous system is present at a cut-surface, even when such a surface is not at the anterior end of the worm. We may perhaps be able to extend this statement, and state that as many heads will develop as there are exposed anterior ends of the nervous system.

In two other cases, at least, a somewhat similar conclusion may be drawn, although it appears that in these cases other organs than the nervous system may be the centres around which the new parts develop. Tornier has shown that when the vertebræ of the tail of the lizard are injured, the new material proliferated by the wounded surfaces serve as centres [1] for the regeneration of new tails; and Barfurth has found that the notochord in the tail of the tadpole plays a similar rôle in the formation of a new tail. These experiments will be more fully described in connection with the formation of double structures, but from what has been said it will be seen that the cases are parallel to that of the earthworm.

Until more has been discovered in regard to the internal factors of regeneration, it would be venturesome to make any general statement based on these few cases, but there is opened here a wide field for experimental work. By eliminating one by one the different organs that are present in the old part, it may be possible to discover much more in regard to the internal conditions that are necessary in order that the process of regeneration may take place.

### THE INFLUENCE OF THE AMOUNT OF NEW MATERIAL

There are certain results connected with the amount of new material which is produced during regeneration, that should be considered in connection with the question of internal factors. It has been pointed out that when one segment only is removed from the anterior end of the earthworm only one new one returns; when two are cut off two come back, and this holds good up to five segments. Beyond this, no matter how many are removed, only five at most come back. The latter result seems to be connected with the amount of material that is formed over the cut-surface before differentiation begins. When only one or two segments have been cut off, the new material that is formed is soon sufficient in amount for the production of one or two new segments, but when three to five are cut off somewhat more material is formed before differentiation begins. When more than five are cut off the new material is at best only sufficient to produce five new ones, and in some cases even a smaller number is formed. This hypothesis assumes that there is a lower limit of size for the formation of new segments below which a segment

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[1] Although it is by no means certain that the results may not be due in part, at least, to injuries to the nervous system.

cannot develop. The interpretation is fully in accordance with what we know to be the case for small pieces of hydra and of other forms that, below a certain minimal size, do not regenerate. The question as to how many segments are formed out of the new part is determined, not only by the amount of new material, but also by the number of segments to be replaced, at least up to five segments. Beyond this limit we may think of the maximum possible number of segments appearing in the new material. That a relation of some sort obtains between the old and the new parts, that may have an influence on the number of the new segments which are formed, is shown by the fact that, when one, two, three, four, or five are cut off, just this number comes back. A sort of completing principle exists as a factor in the result, but when so much has been cut off that the old part cannot complete itself in the new material that is formed, then other factors must determine how many segments will be produced.

In planarians we find a similar phenomenon. If much of the anterior end is cut off, only a head is formed at the anterior cut-surface of the posterior piece, and the intermediate region is absent. I interpret this in the same way as the similar case in the earthworm. As soon as enough new material has been formed for the anterior end to appear, it begins to develop, and since it cannot develop below a certain minimal size, or rather, since the tendency to produce a head approaching the maximum size is stronger than the tendency to produce as much as possible of the missing anterior end, all the new material goes into the new head. In the planarian the possibility of subsequently replacing the missing region behind the head exists, and the intermediate part is later produced, the head being carried farther forward. The same is true of the new posterior end of the earthworm, in which a growing region is established at a very early stage in front of the tip of the tail, but no such growing region is present at the anterior end in the earthworm. These differences appear to be connected with the general phenomena of growth in these forms. In the planarian interstitial growth can take place in any part of the body, hence the possibility of producing a missing region is present in all parts of the worm ; but in the earthworm we never find new segments inter-calated at the anterior end during normal growth, nor does this take place during regeneration. At the posterior end of the earth-worm we find a region of growth in which new segments are produced, and we find the same thing is true in the regeneration of the posterior end. In other words, the growing region in front of the last segment is also regenerated.

It has been found in several forms that pieces below a certain size do not regenerate. In those cases in which a small piece dies soon

after its removal from the rest of the body we have no direct means of knowing whether or not the piece has potentially the power to regenerate, but in some other cases, in which small pieces may be kept alive for some time, they may not regenerate. Furthermore, the regeneration of small pieces that are just above the minimal size is often delayed and is sometimes imperfect. These small pieces seem to meet with a greater difficulty in regenerating than do larger pieces. Peebles has shown that pieces of hydra that measure less than $\frac{1}{6}$ mm. in diameter ($=$ about $\frac{1}{200}$ of the volume of hydra) do not regenerate, although if very small pieces are taken from a developing bud they may regenerate, even when only $\frac{1}{9}$ mm. in diameter. Very small pieces that are, however, just above the minimal size, while they may assume a hydra-like form, produce only one or two tentacles. The failure of the smallest pieces to regenerate is not due to their dying, since they may live for a much longer time than would suffice for larger pieces to regenerate. Isolated tentacles of hydra do not produce new hydras, although they may remain alive for some time. A single tentacle is larger than the minimal piece, so that its failure to regenerate is probably connected with the differentiation of the tentacle, rather than with its size. The lack of power to regenerate in the smallest pieces of hydra cannot be connected with the absence of any special organ, since these pieces contain both ectoderm and endoderm. In tubularia also, Driesch and I have found that pieces below a certain size do not regenerate (Fig. 27). There is likewise in planarians a lower limit of regeneration, even for pieces that contain all the elements which, being present in larger pieces, make regeneration possible. Lillie has found that nucleated pieces of the protozoon stentor fail to regenerate if they are below the minimal size. He places this minimal size at 80 $\mu$. diameter, which he calculates as $\frac{1}{27}$ of the volume of the stentor from which the piece has come. I have obtained a slightly smaller



FIG. 27. — *Tubularia mesembryanthemum*. *A*. Minimal-sized piece that produced a hydranth. *B, C.* Pieces below minimal size. *D.* Ring produced by closing of small piece.

piece that regenerated, and since it came from a larger stentor it represents about $\frac{1}{64}$ of the whole animal. The lack of the power of development of these smallest pieces seems to be due to the absence of sufficient material for the production of the typical form. We can give no other explanation of the phenomenon at present, especially since the pieces contain material that we know from other experiments has the power of producing any part of the organism. The superficial area of small pieces is relatively greater than that of larger pieces,

but there is no evidence that this relation can in any way influence the result. Whether the difference in surface tension could prevent the small piece from assuming the typical form and hold it, as it were, in a spherical form is not known, but there is little probability that this is the explanation of the phenomena.

The regeneration of small pieces of animals and of plants may often fail to take place, because, as Vöchting has pointed out, the injury caused by the cutting may extend so far into the small piece that its repair may be impossible. In other cases there may be an insufficient reserve supply of food stuff, although, if a proportionate form of any size could be produced, it is difficult to see how this could be the case. There can be no doubt, however, that pieces taken from parts of the body that are dependent on other parts for their food, oxygen, etc., will die for lack of these things, and even if they can live for some time their further development may not take place in the absence of sufficient food to carry on the process. After these possibilities have been given due weight, there remain several cases in which there can be little doubt that the failure of a small piece to regenerate is owing to the lack of sufficient material to produce even the smallest possible form for that sort of material, *i.e.* for the organization to be formed on so small a scale.

There are some facts in connection with the regeneration of small pieces of tubularia that have an important bearing on this question of organization size. If long pieces of the stem are cut off, the new hydranth, that develops out of the old tissue at the end of the piece, occupies, within certain limits, a region of definite length. If pieces of the stem are cut off that are only twice the length of the hydranth-forming region, the length of the latter will be reduced to half the length that it has in longer pieces, and if still smaller pieces are cut off, the hydranth-forming region may be reduced, as Driesch has shown, to seventy per cent of the normal length. The hydranths that develop from the smaller pieces have also a reduced number of tentacles, as I have found. It was first shown by Bickford, and later by Driesch, and by myself, that in many cases very short pieces of the stem of tubularia produce *only the distal parts of a hydranth.* This happens most often when the length of the piece is less than the average normal length of the hydranth-forming area, but it may also take place in pieces that are much longer than the minimal size of the least hydranth-forming region. Driesch made the further discovery, which I have confirmed, that pieces from the distal end of the stem are more likely to produce these partial structures than are pieces from the more proximal part. Some of these partial structures are represented in Fig. 28, *C–G.* Sometimes the inner tube, or cœnosarc, which is composed of the two layers of the body, ectoderm and

endoderm, draws away from the chitinous perisarc, as shown in Fig. 28, *B*. A hydranth with a short stalk is then produced. In other cases, Fig. 28, *C*, almost all of the cœnosarc is used up to form the hydranth, and only a short, dome-shaped knob represents the stalk. In still other cases there may be no stalk at all (Fig. 27, *D*), but only the hydranth. Forms like the last two are more often produced from pieces of the
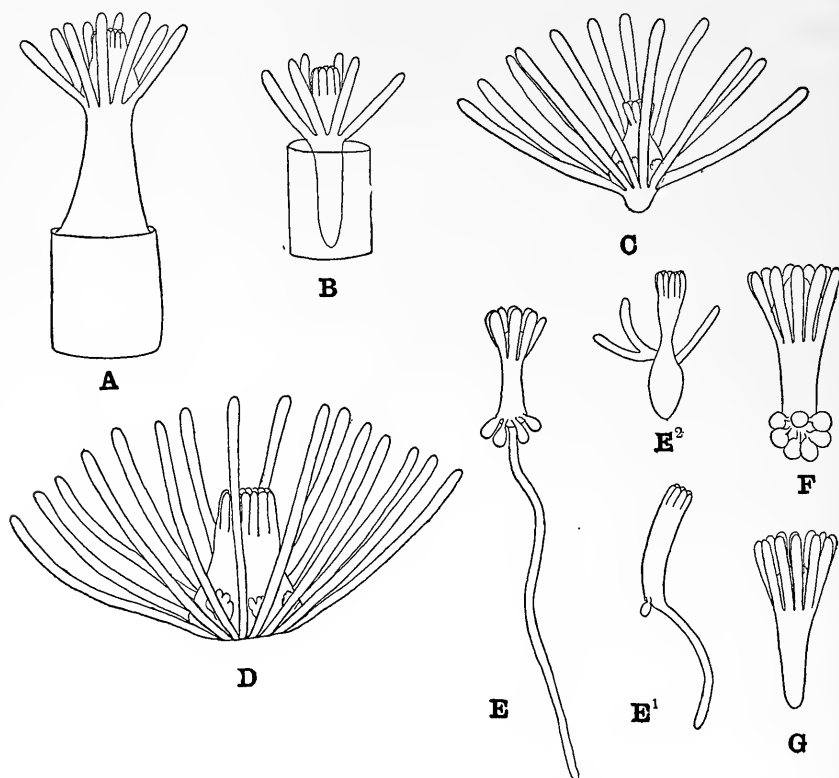


FIG. 28. — *Tubularia mesembryanthemum.* Products of regeneration of short pieces. *A*. Piece that regenerated a hydranth in same way as do longer pieces, but with fewer tentacles. *B*. Pieces whose stem drew away from wall of old perisarc (cylinder in figures). *C*. Hydranth with almost no stalk. *D*. Hydranth without stalk. *E*. Distal part of hydranth with one long proximal tentacle. *E*¹. Similar, but more reduced. *E*². Similar, with two tentacles at side. *F*. Proboscis with reproductive organs. *G*. Proboscis without reproductive organs.

distal end of the stalk. From very small pieces, forms like those shown in Figs. 28, *E–E*², that represent only proboscides with a reduced number of tentacles, are sometimes formed. Reproductive organs may be present at the base of these pieces. A further reduction is shown in Figs. 28, *F*, *G*, that are proboscides with only the distal circle of tentacles ; in one of these, reproductive organs are present around the base. Partial forms more reduced than these have not been found.

If we examine the factors that determine the production of the partial structures, we find, in the first place, that the size of the piece is of the greatest importance. The reduced forms appear most often in pieces that are shorter than the average length of the hydranth-forming area. A second factor is connected with the region of the stem from which the piece is taken. Larger pieces from the distal end produce partial structures, especially hydranths with very short stalks (Fig. 28, *C*), or with none at all (Fig. 28, *D*). There are certain facts connected with this distal region, which lies just behind the hydranth, that should be mentioned in this connection. It was first discovered by Dalyell that a hydranth-head lives for only a limited time, and that when it dies a new head is regenerated from the region behind the old one. The stalk of the new hydranth continues to elongate for some time after the new hydranth has been formed. Whether this continuous growth in the distal end, or the normal formation of a new hydranth by it from time to time, can in any way be connected with the development of partial structures from this region cannot at present be stated. The distal part of the stem contains more of the red-pigment, that gives color to the stem and to the hydranth, than does any other part. Loeb first advanced the view that the red-pigment in the stem acts as a formative substance in Sachs' sense, and determines the production of a new hydranth by accumulating near the cut-end of the piece. Driesch also assumes the red-pigment to be a factor in the result, but supposes that it acts quantitatively, rather than in determining the quality of the result. If this red-pigment acted in the way supposed either by Loeb or by Driesch, it might act as one of the factors in the production of these partial structures. This red-pigment is contained in the form of reddish granules in the cells of the endoderm. The granules are of various sizes, the largest being easily seen even with low powers of the microscope. When a piece of the stem is cut off, the ends close by the drawing in of the cut-edges over the open-end. A circulation of the fluid contained in the piece then begins. In the fluid, globules appear very soon that contain red-pigment granules like those in the endoderm. The globules appear to be endodermal cells, or parts of cells, that are set free in the central cavity. The circulation continues for about twenty-four hours. At about this time one end of the stem becomes reddish, owing to the presence in it of a larger number of red-pigment granules than before. The ridges that are the rudiments of the tentacles appear (Fig. 30, *A*), and a new hydranth very rapidly develops. At the time when the hydranth begins to appear the globules in the circulating fluid disappear. They disappear at the time when the red-pigment of the forming hydranth is rapidly increasing in quantity, and not unnaturally one might suppose that the pigment of the circulating

fluid had been added to the wall where the hydranth is produced. The globules disappear in the region of the new hydranth, but, I think, it can be shown that they do not form any essential part of the hydranth. They may be found stuck together in a ball that lies in the digestive tract of the new hydranth, and when the hydranth is fully formed the pigment is ejected, as Stevens has shown, through the mouth.

The development of the new hydranth begins several hours before the red-pigment globules have disappeared from the circulation. The walls in the region of the future hydranth begin to thicken, and, later, pigment develops in the endoderm of this region. The new pigment is formed in the new cells of the endoderm, and does not come from the circulating globules, as shown by the development of very short pieces of the stem. In these the amount of new pigment that develops in the new hydranth may be far greater than that in the whole original piece (Fig. 30, *D*), and in this case there can be no question but that new pigment is made in the endodermal cells of the hydranth. The formation of a hydranth, that usually takes place after another twenty-four hours, from the basal end of a long piece, shows that a hydranth may develop when there are no granules in the circulating fluid. These basal hydranths may contain as much pigment as do the distal ones.

Driesch suggested that the red-pigment in the circulating fluid determines quantitatively by its presence how much of a hydranth is formed, or the size of the hydranth in relation to the rest of the piece. There seems to be no evidence in favor of this view and much against it. Loeb has not stated specifically whether he means that it is the pigment in the circulating fluid or that in the walls which acts as a formative stuff; the presumption is that he meant the latter. An examination of the piece during regeneration gives no evidence in favor of the view that the pigment moves into the region of the new hydranth. On the contrary, it remains constant in amount at all points except where the new hydranth is developing, and there is in this region unquestionably a large development of new pigment.

The evidence for and against the idea that the red-pigment of tubularia is a formative stuff, or even building material, has been considered at some length, because it is the only case in which the hypothetical formative stuff has been definitely located in a specific, recognizable substance that can be followed during the process of regeneration. It is well, I think, to give the question full consideration, especially as the hypothesis often appears to give an easy solution of some of the problems of regeneration. In a later chapter the subject will be more fully treated.

Since the red-pigment hypothesis does not explain the phenomenon of the formation of the partial structures in tubularia, we must look for another explanation. As the matter stands at present we can only assume that there is a *predisposition* of a very small piece to form a larger partial structure than a smaller whole one. This problem of the method of development of small pieces of the stem of tubularia is further complicated by the development in many cases of double hydranths, or double parts of hydranths, as shown in Fig. 29, *A–E*.
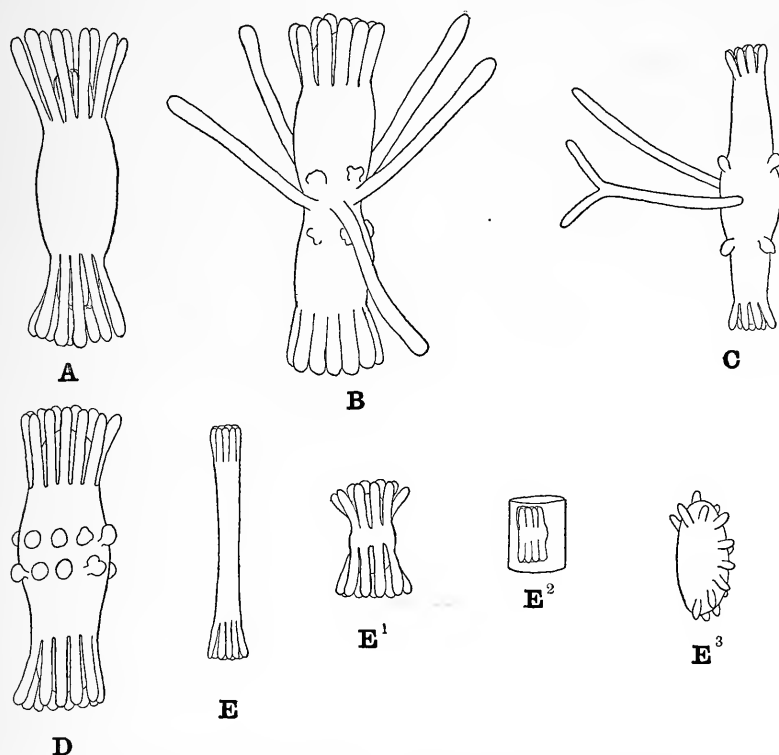


FIG. 29. — *Tubularia mesembryanthemum.* *A.* Short piece with hydranth at each end. *B.* Double piece with one circle of proximal tentacles. *C.* Double piece with only two proximal tentacles. *D.* Double proboscis with two sets of reproductive organs. *E–E³.* Double proboscis.

The first form (Fig. 29, *A*) shows two hydranths turned in opposite directions, that are united at their bases. Another form has only a single circle of proximal tentacles between the two proboscides (Fig. 29, *B–C*). In other forms there are only two proboscides, each with its reproductive organs (Fig. 29, *D*), and often there are simply two proboscides united at the base (Fig. 29, *E–E³*). It is the rule, even in longer pieces, that a hydranth appears at each end of the piece, if the piece is suspended or even lies on the bottom of the water; but

in all these cases the basal hydranth develops about twenty-four hours after the apical one. In the short pieces, however, the two ends develop at the same time, although the development of all the short pieces, whatever structures they may produce, whether single or double, is delayed, and the hydranths may not appear until after the long pieces have produced their basal hydranths. In these double
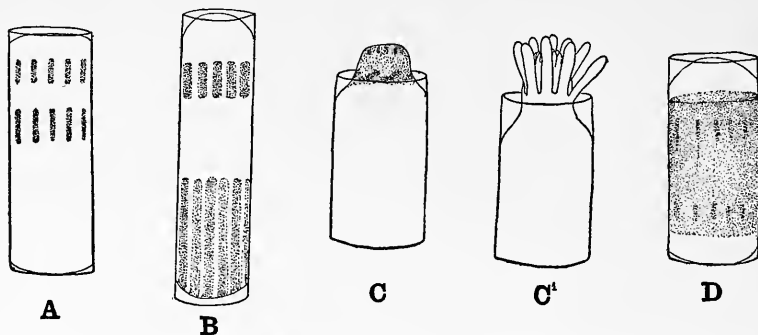


FIG. 30. — *Tubularia mesembryanthemum.* *A.* Short piece with reduced hydranth-region. *B.* Piece from distal end of stalk producing a hydranth without a stalk (see Fig. 27, *D*). *C.* Piece producing hydranth as outgrowth of end. *C*[1]. Later stage of last. *D.* Short piece producing double proboscis (see Fig. 28, *E*).

structures both ends develop at the same time (Fig. 30, *D*). If we suppose the influences that start the development of the piece begin first at the distal end, the region affected will lie so near to the proximal end of the piece that the development at this end may be hastened, and under these circumstances the region of new formation will be shared by the two hydranths. The factors that determine that a larger, partial structure is formed in preference to a smaller whole one will no doubt be found to be the same in these double structures and in the single ones.

### THE INFLUENCE OF THE OLD PARTS ON THE NEW

One of the most striking and general facts connected with the phenomenon of regeneration is that the new part that is built up on the exposed surface is like the part removed. This suggests that an influence of some sort starts from the old part and changes the part immediately in contact with it into a structure that completes the old part in that region. We can imagine that the new part that has been changed in this way may act on the new part just beyond it, and so step by step the new part may be differentiated. It is not difficult to show that the phenomenon is really more complicated than this, and that other factors are also acting on the new part; but, nevertheless, that the old part has some such influence is probable. Under certain conditions, however, this influence may be counteracted by other fac-

tors, and something different from the part removed may be formed. One example of this sort has already been discussed, namely, that in which after the removal of much of the anterior end of the earthworm or of a planarian, only the distal end comes back. Another case is that in which something different from the part removed is regenerated. If the tip of the eye of the hermit-crab or of other crustaceans is cut off a new eye is regenerated, but if the eye-stalk is cut off near its base an antenna-like organ develops. Herbst has suggested that the presence of the ganglion at the end of the stalk accounts for the regeneration of a new eye, when only the tip of the stalk is cut off. In the absence of the ganglion at the cut-edge the stalk does not produce an eye, but an antenna, as is shown when the eye-stalk is cut off near the base. The factors that determine the development of an antenna instead of an eye have not been discovered. Przibram has shown that when the third maxilliped of portunas, carcinas, or of other crustaceans is cut off near the base, the new appendage that develops is different from the one removed, and resembles a leg in many ways, but if the animal is kept until it has moulted several times the appendage becomes more and more like the part removed. Another remarkable case has also been described by Przibram for *Alpheus platyrrhynchus*. In this decapod, the claws of the first pair of legs are different from each other, one being much larger than the other and having a different structure.[1] If the larger claw is thrown off at its breaking-joint, and the smaller one left intact, the latter at the next moult (or sometimes after two moults) changes into the characteristic larger claw and the newly regenerated claw is like the smaller one. If the experiment is repeated on this same animal, *i.e.* if the newly acquired large claw is removed, then at the next moult the smaller claw becomes the larger one and the new claw becomes the smaller one — the conditions now being the same once more as at the beginning. If both claws of an animal are thrown off at the same time, two new claws regenerate that are both of the same size, and each is a small copy of the claw that was removed. As yet no experiments have been made that show what factors regulate the development of each kind of claw.

Returning again to the question of the regeneration of parts similar to the ones removed, there are some interesting results that Peebles has obtained in the colonial hydroids, podocoryne and hydractinia. These colonies consist of three principal sorts of individuals: the nutritive, the reproductive, and the protective zooids. Peebles has found that if the stalks of these zooids are cut into pieces, each produces the same kind of zooid as was originally carried by that stalk. Pieces of the stem of the nutritive zooid produce new nutritive zooids

[1] In normal animals some have the right claw the larger and some the left.

at the anterior end of the piece, and sometimes also at the basal end. A similar statement may be made for each of the other kinds. Another method of regeneration sometimes takes place, when, for instance, a piece of the stalk of a nutritive individual is left undisturbed without being supplied with fresh water. It sends out root-like stolons instead of producing a new zooid. The stolons appear first at the ends of the piece, but may later also appear at several points along the piece. They make a delicate network, and the original piece may entirely disappear in the stolons. After several days new feeding zooids grow out at right angles to the stolon network. Pieces of the stalk of protective zooids may also produce stolons, but they spread less slowly, and the formation of new individuals was not observed. In one case a piece of a reproductive zooid made a short stolon, and from it arose a new individual that seemed to be a nutritive zooid. If the latter result proves to be true, we see that a piece may produce a new part that is of a different kind from that of which the piece itself was once a part, but this is brought about by the formation of a stolon that is itself one of the characteristic structures by means of which these colonial forms produce new nutritive zooids. In this case there is a return of the piece to a simpler form, the stolon, and, acting on this, the factors that produce nutritive zooids may bring about new nutritive zooids. The influence of the old structure is lost when the piece assumes a new character.

Another series of experiments gives an insight into an internal factor of regeneration that may prove, I think, to be one of some importance and help in interpreting certain phenomena. If the head-end of a planarian is cut off, the posterior piece split along the middle line, and one side cut off, just above the lower end of the longitudinal cut, as shown in Fig. 31, *A*, it will be found that, if the long and the short sides are kept from uniting along the middle line, each half will produce a new head on its anterior surface (Fig. 31, *C*). If the two halves grow together, and the anterior surface of the shorter piece becomes connected with the anterior surface of the longer piece by means of the new tissue that develops along the inner side of the latter (Fig. 30, *B*), then a head appears only on the anterior half. The development of a head on the shorter half is prevented by the establishment of a connection with the new side. Sometimes an abortive attempt to produce a head is made, but the posterior surface fails to produce anything more than a pointed outgrowth. If we attempt to picture to ourselves how this influence of the new side on the posterior surface is brought about, we can, I think, most easily conceive the influence to be due to some kind of tension or pull of the new material which is of such a sort that it restrains the development of a head at a more posterior

level. We can picture to ourselves the same kind of process taking place in the regeneration of the tail of a fish from an oblique surface. The maximum rate of growth is found over that part of the cut-sur-
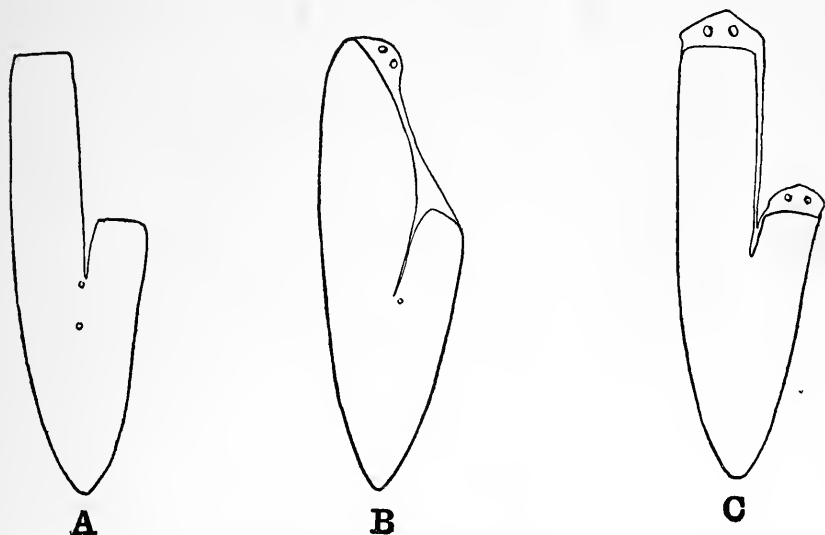


FIG. 31.—*Planaria lugubris.* *A.* Showing how worm was operated upon. *B.* A single head regenerated at anterior cross-cut. It was united by a line of new tissue along the side of the long half-piece with the new tissue at the anterior end of the short half-piece. The two half-pieces reunited along the middle line. *C.* Two heads regenerated, one from each half cross-cut. The two half-pieces were kept apart along the middle line.

face that is nearer the base of the tail (Fig. 40). At all other points the growth is retarded, or held in check, and it can be shown that the suppression is connected with the formation of the typical form of the tail in the new part. If we cannot actually demonstrate at present that this is due to some sort of tension between the different parts which regulates the growth, we find, nevertheless, that it is by means of some such idea as this that we can form a clearer conception of how such a relation of the parts to each other is established. In a later chapter this subject will be dealt with more fully.

### THE INFLUENCE OF THE NUCLEUS ON REGENERATION

The influence of the nucleus on the process of regeneration has been shown in a number of unicellular forms. It was first observed by Brandt in 1877 that pieces of *Actinosphærium eichhornii* that contain a nucleus assume the characteristic form, but pieces without a nucleus fail to do so. Schmitz ('79) found that when the wall of the many-celled siphonocladus is broken, the protoplasm rounds up into balls, some of which contain one or more nuclei, while

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others may be without nuclei. The nucleated pieces produce a new membrane, and later become typical organisms, but non-nucleated pieces do not form a new membrane, and soon disintegrate. Nussbaum ('84, '86) cut into pieces the ciliate infusoria, oxytricha and gastrostyla. Those pieces that contained a nucleus quickly regenerated a new whole organism of smaller size, that had the power of further reproduction, while the pieces that did not contain a part of the nucleus showed no evidence of regeneration; and, although they continued to move about for as much as two days, they subsequently disintegrated. Gruber obtained the same result on another ciliate infusorian, *Stentor cœruleus*. He found that, although the non-nucleated pieces close over the cut-surface, and move about for some time, they eventually die. He further showed that a non-nucleated piece containing a portion of a new peristome in process of formation will continue to develop this new peristome, although a new peristome is never produced by a non-nucleated piece under other circumstances. He believes that if the new peristome has begun to be formed under the influence of the old nucleus, it may continue its development after the piece is severed from its connection with the nucleus. A non-nucleated piece containing a part of the *old* peristome does not produce a new peristome from the old piece. Gruber observed that a non-nucleated piece of amœba behaves differently from a nucleated piece, and dies after a time.

Klebs found that when certain algæ are put into a solution that does not seriously injure them, but causes the protoplasm to contract into balls, some of these contain nuclei, others not. If, for instance, threads of zygnema, or of spirogyra, are placed in a 16 per cent solution of sugar, the protoplasm of each cell breaks up into one or more clumps, some with nuclei, others without. Both kinds may remain alive for a time; some of the non-nucleated pieces may live for even six weeks. The nucleated pieces surround themselves at once, when returned to water, with a new cellulose wall, but the non-nucleated pieces remain naked. The latter can, nevertheless, produce in the sunlight new starch that is used up in the dark and is made anew on the return to light.[1]

Balbiani ('88) found that non-nucleated pieces of cytrostomum, trachelus, and protodon failed to regenerate, and Verworn ('89 and '92) obtained similar results on several other protozoa. Similar facts have been made out by Hofer ('89), Haberlandt and Gerassimoff ('90). Palla ('90) found that in certain cases non-nucleated pieces, especially those from cells in growing regions, can produce a new cell wall; while more recently Townsend ('97) has shown in

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[1] In other plants, fumaria, for example, non-nucleated pieces do not seem to be able to make new starch after using up that which they contain at first.

several forms that non-nucleated pieces do not produce a new cell wall unless they are connected by protoplasmic threads with nucleated pieces. The most delicate connection suffices to enable a non-nucleated piece to make a cell wall, even when the nucleated piece lies in one cell and the non-nucleated in another, the two being connected by a thread of protoplasm that passes through the intervening wall.

If we examine somewhat more in detail some of these cases, we find that when a form like stylonychia is cut into three pieces, the two end-pieces without a nucleus fail to regenerate, while the central piece makes a new entire organism of smaller size. If stentor is cut into three pieces, each piece containing one or more nodes of the macronucleus, each produces a new stentor. If, however, a piece is cut off so that it does not contain a part of the macronucleus, it fails to regenerate. Verworn ('95) succeeded in removing the central capsule with its contained nucleus from the large radiolarian, *Thallasicolla nucleata*. The non-nucleated animal remained alive for some time, but eventually died. The nucleated capsule developed a new outer zone with processes like those in the normal animal. If the nucleus is taken from the capsule, the capsule dies, but shows some traces of the formation of an outer zone. If the protoplasm is removed as far as possible from around the nucleus, the latter does not regenerate new protoplasm, but dies after a time. Verworn concludes that the protoplasm cannot carry on all its normal functions without the nucleus, or the nucleus without the protoplasm.

These experiments sufficiently demonstrate that non-nucleated pieces are unable to regenerate. If we attempt to examine further into the meaning of the phenomenon, we find a few things that appear to have a bearing on the result. The behavior of the non-nucleated pieces shows that the metabolism of the cell has been changed after the removal of the nucleus. In some cases the protoplasm is not able to carry out the process of digestion of the included food substances. This process may be due to some interchange that goes on between the nucleus and the protoplasm, which is stopped by the removal of the nucleus, and, in consequence, the metabolism of the cell is changed. The lack of regenerative power may be due to this change in the metabolism. It cannot be claimed, however, that the result is due to a lack of energy in the pieces, for the incessant motion of the cilia in some kinds of pieces, that goes on for several days, shows that a large store of energy is present. Unfortunately, we do not know enough of the relation that subsists between the nucleus and the protoplasm to be able to state to what the lack of regenerative power is due.

Loeb ('99) has suggested that the lack of power of non-nucleated

pieces may be due to a lack of oxidation. The nucleus contains substances which, according to Spitzer, are favorable to the process of oxidation. When the nucleus is removed, the oxidation is supposed by Loeb to be too low to allow the process of regeneration to take place. In support of this view, he points out that while non-nucleated pieces of infusoria live for only two or three days, non-nucleated pieces of plants containing chlorophyl may be kept alive for five or six weeks. Non-nucleated pieces containing chlorophyl can obtain a supply of oxygen, owing to the breaking down of carbon dioxide in the chlorophyl-bodies, and the consequent setting free of oxygen. It should be pointed out, on the other hand, as opposed to Loeb's view, that non-nucleated pieces of amœba have been kept alive for fourteen days; and that despite the better oxidation that may take place in non-nucleated pieces of plants, regeneration does not take place.

It has been found that non-nucleated pieces of the egg of the sea-urchin do not segment or develop, and the result is the same whether the pieces come from fertilized or unfertilized eggs. If, however, a spermatozoon enters one of these pieces, the piece will segment, and, as Boveri and later Wilson have shown, it will produce an embryo.

Boveri also tried fertilizing a non-nucleated piece of the egg of one species of sea-urchin with a spermatozoon of another species. He found that the embryo that develops is of the type of the species from which the spermatozoon has come, and he concluded that the nucleus determines the character of the larva, and that the protoplasm has no influence on the form. The evidence from which Boveri drew his conclusion is not beyond question. It has been shown by Seeliger ('95) and myself ('95) that if whole eggs of the species *Sphærechinus granularis*, used by Boveri, are fertilized by the spermatozoa of the other species, *Echinus microtuberculatus*, there is great variability in the form of the resulting larvæ. Most of them are intermediate in character between the types of larvæ of the two species, but a few of them are like the paternal type. Vernon ('99) has more recently shown that the character of hybrids is dependent upon the ripeness of the sexual products of the two parents. If, for instance, the eggs (sphærechinus) are at the minimum of maturity, the hybrids are more like the male (strongylocentrotus).

It remains, therefore, still to be shown whether or not the protoplasm has any influence on the form of larva that comes from a non-nucleated piece, fertilized by a spermatozoon of another species. That the nucleus of the male does have an influence on the form of the animal is abundantly shown by the inheritance of the peculiarities of the father through the chromatin of the spermatozoon.

## THE CLOSING IN OF CUT-EDGES

One of the most familiar changes that takes place when a cut-edge is exposed involves the rapid covering over of the exposed tissues. This takes place from the margin of the wound, and a layer of cells, usually the ectoderm at first, covers the surface. The closing in is brought about in many forms by the contraction of the muscles of the outer wall of the body. This seems to be the case in the earthworm and in the planarian, as well as in other animals, such for instance as the starfish, holothurian, etc. But in addition to this purely muscular contraction another process takes place, that is less conspicuous in forms in which the muscles bring about the first closing, but which is evident in forms in which the muscles are absent or little developed. I am able to cite two striking cases that have come under my own observation. When a piece is cut from the stem of tubularia, the ends close in twenty minutes to half an hour. The body wall, the cœnosarc, composed of the two layers of ectoderm and endoderm, withdraws a little from the cut-edge of the outer hard tube, or perisarc, that covers the stem, and then begins to draw across the open end. A perfectly smooth, clean edge is formed that advances from all points to the centre, where the final closing takes place. The closing is not due to an arching over of the cœnosarc, but the thin plate is formed standing nearly at right angles to the outer tube. This plate is composed of two layers of cells, of which there are a number of rows arranged concentrically between the centre and the outer edge. In the absence of muscle-fibres in the stem, the result cannot be due to a muscular contraction, and even if short fibres existed the transportation of cells entirely across the open end would speak against this interpretation.[1] Since the closing over takes place without any support, we cannot suppose the process to be due to any sort of cytotropic effect. The closing takes place equally well in diluted sea water and in stronger solutions. The method of withdrawal of the cells, as best seen when longitudinal pieces are studied, resembles very much the withdrawal or contraction of protoplasmic processes in the protozoa, and so far as one can judge from resemblances of this sort, the two processes appear to be the same.

This closing in of the cut-surface, while a preliminary step in the process of regeneration, cannot, I think, be regarded as a part of the regeneration in a strict sense. That the two processes are not dependent on the same internal factors is shown by the following experiments: If a bunch of tubularia is kept in an aquarium, it will

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[1] I have found that the closing in takes place equally well when one per cent of KCl is added to the sea water. This salt has, as Loeb has shown, an inhibiting effect on muscular contractility, — not, however, on amœboid movements.

produce new heads two or three times and then cease, and if after the last-formed heads have died, pieces of the stem are cut off, they close as readily as do pieces from fresh hydroids. Moreover, at certain times of year the species *Tubularia* (*Parypha*) *crocea* lose their heads, and only the stalks remain. Pieces of these stalks will not regenerate new heads, at this time, although they close in as quickly as do pieces at other times of the year when the heads are present and when new ones regenerate.

Another equally good illustration of what seems to be the same phenomenon is found in the closing in of wounded surfaces in the young tadpole embryos. If embryos are taken from the jelly membranes, or even after they have been set free, and cut in half, each piece quickly covers over the wounded surface by means of the ectodermal cells. A much more striking illustration of this closing over in the young tadpole is obtained by cutting, with a pair of small scissors, a large piece from the side. The area may be a fourth or more of the entire side, and yet it may be closed over in an amazingly short time. Half an hour or an hour often suffices to cover a large exposed surface. In this case also the wound is covered not by individual cells wandering over the exposed surface, but by a steady advance of the smooth edge of the ectoderm toward a central point. The process is so similar to that which takes place in tubularia that little doubt can remain as to the two being due to the same factors. As there are no muscle fibres present in the part of the frog's embryo from which the piece is cut off, the result cannot be due to muscular contraction, but appears to be a contractile phenomenon similar to that in tubularia. Even the small piece that is cut from the side of the body shows the same phenomenon. At first it suddenly bends outwards owing to some physical difference between the inner and the outer parts of the piece. Then the edges thicken, bend in, and begin their advance over the inner tissues. The process is seldom completed, since there appears to be a limit to which the ectoderm can be stretched as the edges advance. A most striking phenomenon both in pieces of tubularia and of the frog's embryo is the entire absence of dead material at the wounded surface. No sooner is the operation performed than the advance begins, and there is not a trace of dying cells or parts of cells to be seen.

# CHAPTER IV

## REGENERATION IN PLANTS

THE series of experiments that Vöchting has carried out on the regeneration of the higher plants are so much more complete than all previous experiments, and his analysis of the problems concerning the factors that influence regeneration is so much more exact than any other attempts in this direction, that we may profitably confine our attention largely to his results. Many of his experiments were made with young twigs or shoots of the willow (salix), which, after the removal of the leaves, were suspended in a glass jar containing air saturated with water. Under these circumstances the pieces produced new shoots from the buds (leaf-buds) that are present near the point at which the leaves were attached, and new roots, in part from root-buds, that are also present on the stem.

If the piece is suspended in a vertical position with its *apex upward* (Fig. 32, *A*), small swellings appear after three or four days near the lower, *i.e.* the basal, end of the piece. These break through quickly and grow out as roots. If a leaf-bud is present near the basal end of the piece, the first roots appear at the side of or under this; later others appear around the same region. The first roots to appear under these conditions come from pre-formed root rudiments, the others are, in part at least, new, adventitious roots. If the lower end of the cut is made through the lower part of a long internode, *i.e.* just *above* a bud, the roots appear as a rule only near the cut-end, and few if any of the roots develop at the first bud above this region. In many cases there is formed over the basal cut-surface, in the region of the cambium, a thickening, or callus, and not infrequently from this also one or more roots may develop. The direction taken by the new roots is variable, being sometimes downward, sometimes more or less nearly at right angles to the stem.

While these changes have been taking place at the base, the leaf-buds at the apical end have begun to develop. One, two, three, four, or even five of the higher buds begin to elongate, the number and extent of development depending on the length of the piece. The topmost or apical bud grows fastest, and the others grow in the order of their position. In the region below the lowest bud that develops

there may be one or more buds that do not grow; but if the piece is cut in two just above these buds, they will then grow out.

The results show that at the base of the piece the same factors that bring about the development of the rudiments of preëxisting roots also cause the development of new roots, if the lower end is in a region in which there are no rudiments of roots present. The
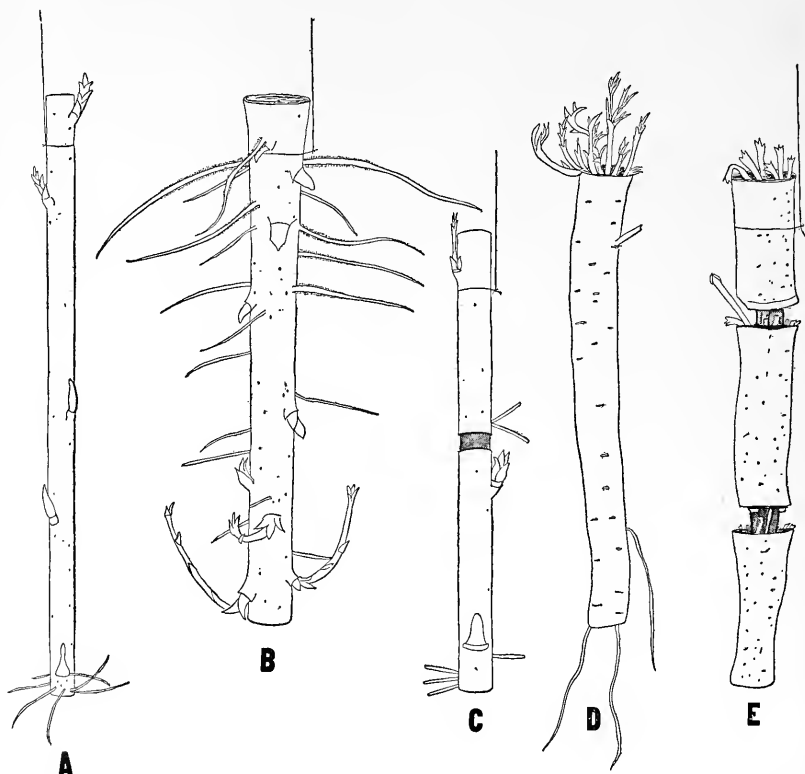


FIG. 32. — After Vöchting. *A*. Piece of willow cut off in July, suspended in moist atmosphere with apex upward. *B*. Older piece of willow (cut off in March) suspended in moist atmosphere with apex downward. *C*. Piece of willow with a ring removed from middle. Apex upward. *D*. Piece of root of *Populus dilatata*. Basal end upward. Shoots from basal callus. *E*. Piece of root of same with two rings removed. New shoots develop from basal callus, and from basal end of each ring.

influence that produces the new roots is confined to the basal part of the piece. In the apical part of the piece there are no adventitious structures produced, but a longer region is active, and several pre-formed leaf-buds begin to elongate. The topmost shoot grows faster than the others, showing that the influence that produces the growth is stronger near the apical end than at points further removed.

If another piece of a willow stem be placed under the same condi-

tions, but suspended with the basal end uppermost, results that are in many respects similar to the last are obtained. Roots appear around the base of the piece, *i.e.* around the upper end, and the leaf-buds that develop are those that stand nearest to the apical, at present the lower, end of the piece.

These results seem to indicate that, in the main, the chief factors that determine the growth of the new part are internal ones; and although internal factors do appear to be the dominating ones, since roots appear in both cases at the base and shoots at the apex, yet it would be wrong to conclude that gravity has no influence at all on the result. In fact, other experiments show that it does have an influence.

If an older branch (8–12 mm. in diameter) is cut off and hung up with its *base upward*, the result is somewhat different from that with younger branches. The roots appear along the entire length of the piece, as shown in Fig. 32, *B*; the largest are those near the base, and they decrease in size toward the apex of the piece. It is also noticeable that all the roots come from preëxisting root-buds, and no adventitious roots are formed, even at the base. The leaf-buds that develop are those arising near the apex, as in the last experiments. They bend upward as they grow longer. A comparison of the results obtained from younger and older pieces may, at first, seem to show that the difference in their development is due to the greater amount of reserve food stuff in the older piece, and Vöchting thinks it probable that this influence may account for the strength, length, and even for the number of roots that develop, but he believes that it is improbable that their mode of origin and their location can be so determined. Furthermore, the development of new roots around the base of the younger piece can hardly be explained as due to the *absence* of food stuff. The explanation of the production of a smaller number of roots in a young piece is that its tissues are less highly specialized, its buds less advanced, and the piece itself is in a lower stage of development. Another explanation must be found for the greater number of roots that develop in the older piece. This is due, as Vöchting tries to show, in part to the influence of gravity on the piece.

Vöchting's general conclusion is that "the force or forces that determine the *polar differences* in the piece are most evident and most energetic in very young twigs; that this difference decreases with the age of the twig whose leaf-buds and root-buds become further developed. It is clear that the new roots of *young twigs* could appear in corresponding number and strength in exactly the same regions in which they grow out from pre-formed buds of *a year-old twig*. Since this does not occur, and since the roots appear only near the base of young twigs, the explanation must be that the innate polar forces

act more energetically in young twigs, and the buds that develop in the older twigs must arise in antagonism to the action of this force." The polar difference between apex and base is present, nevertheless, as Vöchting's experiments show, even in quite old pieces.

A series of experiments was carried out with the internodes of several plants in order to see if, in the absence of pre-formed buds, new buds
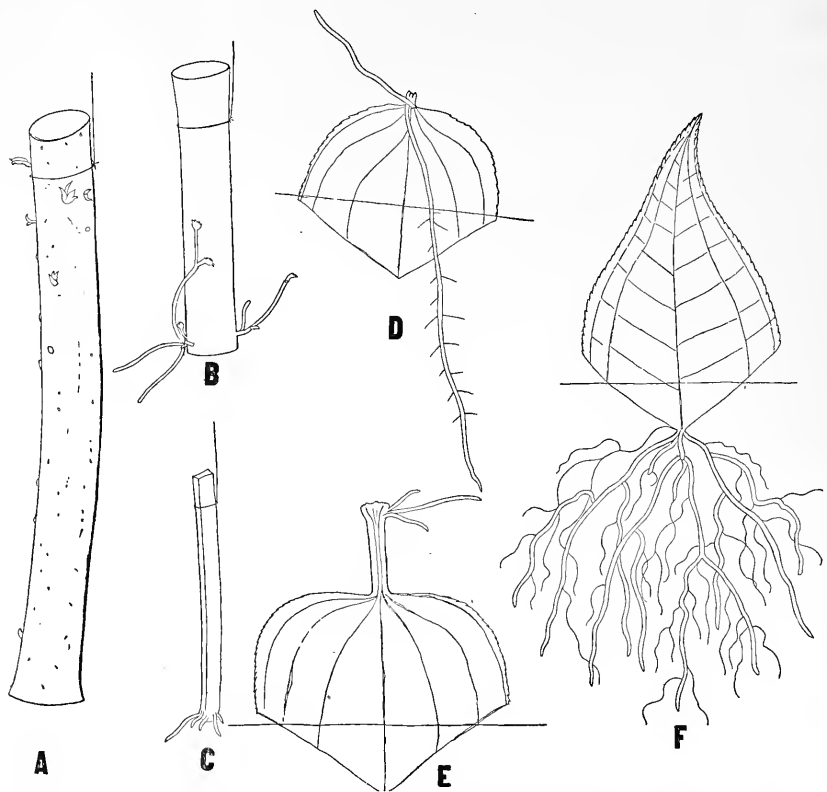


Fig. 33.—After Vöchting. *A*. Internodal piece of *Begonia discolor*. Apex upward. *B*. Same with apex downward. *C*. Internodal piece of *Heterocentron diversifolium*. Apex upward. *D, E*. Pieces of leaf of *Heterocentron diversifolium*. Apex downward. *F*. Same with apex upward. *D, E, F*. Same planted in earth.

would develop. The experiments were undertaken in order to ascertain whether the same polarity, exhibited by longer pieces, would be also found in internodal pieces. In most plants pieces of this kind do not produce new structures, but in *Heterocentron diversifolium* an internode produces roots at its basal end without regard to the position of the piece (Fig. 33, *C*). Leaves do not appear on these pieces. On the other hand internodes of *Begonia discolor* give the opposite result, as

shown in Fig. 33, *A*, *B*. In this case leaf-buds appear at the apex of the internodal piece (Fig. 33, *A*), even when the apical end is downward (Fig. 33, *B*). From the bases of the new shoots roots may then develop, as also shown in the figure (Fig. 33, *B*). Vöchting concludes that the same polarity that is a characteristic feature of longer pieces is also present in internodal pieces.

It is not necessary to separate completely portions of the stem in order to produce roots near one end and shoots near the other. If a ring, including the cambium layer, is cut from the piece, as indicated in Fig. 32, *C*, the part above and the part below act independently of each other, and each behaves as a separate piece. In various other ways the same result may be obtained, as by simply making an incision in the stem at one side, or by partially splitting off parts of the stem (Fig. 34, *C*).

If instead of a piece of the stem, a piece of a root is removed, the results are as follows. [1] It should be remembered that the basal end of a root is the part nearer the stem, the apex is the part nearer the apex of the root. If pieces of the root of the poplar, *Populus dilatata*, are suspended vertically (Fig. 32, *D*) in a moist chamber, a covering of new cells, a callus, appears over the cutends. From the basal callus numerous leaf-shoots may develop. Pieces of large roots may produce over a hundred of these shoots from a single basal callus. In some cases adventitious shoots may also arise from the side of the root near the basal end. Roots develop from the callus over the apical end; less often from the sides near the end. If a similar piece of root is suspended with its apical end upward, the new shoots arise as before over the basal end, that is now turned downwards.

The leaves of some plants, as has long been known, are able to produce new plants. The begonias are especially well suited for experiments of this kind. A piece of the stalk of a leaf suspended in a moist atmosphere produces roots near its base. In most cases the opposite end of the stalk, *i.e.* the end nearest the leaf, putrefies and slowly dies toward the base. Near the base there may arise, before the breaking down of the piece has reached this point, leaf-buds that arise just above the first-formed roots. When these new shoots have reached a certain size they may produce their own roots at or near the base. If, however, a portion of the leaf is left attached to the leaf-stalk (Fig. 35, *A*), new roots arise near the basal end of the stalk, and later shoots grow out near the point of union of the leaf and its stalk at the point where the veins of the leaf come off. These shoots produce roots of their own near the base, and roots may also appear on the part of the leaf-stalk near its union with the lamina. If a

[1] Knight obtained similar results in 1809.

part of the mid-vein, or of any large vein of the leaf, is cut out, leaving a part of the lamina on each side (Fig. 35, *B*), and the piece is suspended vertically, roots appear on the basal end of the vein, and in the same region one or more shoots arise.

Leaves of heterocentron with the stalk attached, if kept in diffuse light, produce roots along the stalk, especially near the basal end, but shoots do not appear, even after five months (Fig. 35, *C*).

These experiments show that the leaves do not exhibit the same polar relations that are shown by pieces of the stem and root. Vöchting points out that the results may be explained in either of two ways. The stem and the root have in general an unlimited growth with a vegetative point at the apex. The leaf has only a limited growth. Its cells form permanent tissue, hence the leaf does not produce a new plant from its outer part. The second possibility is this : the phenomenon is connected with the symmetrical relations that different structures possess. Stem and root are symmetrical in two or more directions, the leaf on the other hand is a flat structure with one plane of symmetry, and even symmetry in one plane may be absent. If the leaf could produce shoots at its apex and roots at its base, from the semilunar fibrovascular bundle of the leaf, then an individual (the leaf) with its single plane of symmetry would produce shoots and roots that are symmetrical in two planes. Such a result would be so anomalous that one may well doubt the possibility of its coming into existence.[1]

Later, Vöchting attempted to see if the same relation found in the leaf would hold for other organs that have a limited growth. He found that such structures, as spines, for example, produce both shoots and roots near the base, as do leaves.

These experiments of Vöchting on the regeneration of pieces of the higher plants show that a piece possesses an innate polarity, or "force," as Vöchting sometimes calls it (although he explicitly states that he does not use the word "force" in its strict, physical sense). It does not follow, of course, that external conditions may not also influence the regeneration, but in those experiments in which the pieces were freely suspended in a moist atmosphere, the external factors are as far as possible excluded, so that the effect of the innate tendencies are most clearly seen. In another series of experiments the influence of external conditions on the regeneration was especially

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[1] Vöchting points out that a parallel case is found in certain conifers. In these there arise from a vertical many-sided main stem whorls of side branches that are symmetrical in one plane. These lateral branches, if cut off and planted, produce new roots and new branches, but the latter are always side-branches, like the parts from which they arise. They never produce a normal main axis. Nevertheless, although these branches cannot themselves produce a main shoot, a callus may be formed at the base of the piece, and from this a new main stem may arise.

studied. This analysis that Vöchting has made of the problem of regeneration is in the highest degree instructive, since it shows how several factors, — some internal, others external, — take a hand in the result; and it is only possible to unravel the problem by combining different experiments carried out in such a manner that one by one the different factors at work are separated.

If a piece of a young stem of *Salix viminalis* is suspended vertically in a moist atmosphere, with the lower end in water (for $\frac{3}{4}$ of a centimetre), and the piece kept in the dark, the result is, in the main, the same as when similar pieces are suspended in moist air without coming into contact with water. Roots arise near the base, and shoots near the apex, without regard to which end is in the water.

If the same experiment is repeated in ordinary air, *i.e.* air not saturated with water, the result is somewhat different. If the twig is suspended vertically with its *apex upward*, roots soon appear on the basal end that is in the water, but no roots develop above the water. Small protuberances may appear above the water in the places at which roots would develop if the piece were surrounded by a moist atmosphere, but they do not break through the bark. If the piece is then covered by a jar containing air saturated with moisture, these protuberances may become roots. It is clear, therefore, that the dryness of the air has prevented their development.

If a similar twig is suspended (in the air) with its *apex downward*, and the lower end in water, root protuberances appear, at first, only around the base, *i.e.* at the upper end. Under the water, at the apical end, small and weak roots may develop, or may even not appear at all.

These results agree, in the main, with those in which the piece is surrounded by moist air, and give evidence of an inner polarity that is an important factor in the regeneration. The results show that in a piece with the basal end in water and the rest of the piece in the air the tendency to produce roots above the water is suppressed by the dryness of the air. In an inverted piece, however, with the apex in water, the innate tendency to produce roots at the basal end is strong enough to overcome the effect of the dryness of the air to suppress their development. The abundance of water absorbed by the apex of the piece makes the development of the roots possible under these conditions despite the dryness of the air.[1]

There is another factor connected with the submergence of the end of the stem in water that can be shown by putting a longer part of the end under the water. Neither roots, if it is a basal end, nor leaf-buds, if it is an apical end, appear on the deeper parts of the submerged end. This is due, in all probability, to the insufficiency

[1] A piece suspended in ordinary air dries up without producing any new structures.

of oxygen in the water, and as a result the buds are prevented from developing.

It can be shown that light has also an influence on the regeneration of pieces, and that it has a stronger influence on some plants than on others. In some plants roots develop only on that side of the stem that is less illuminated. In *Lepismium radicans*, for instance, adventitious roots are produced by the plant even in dry air. Pieces of the stem can produce roots on either the upper or the lower surface, according to which side is less illuminated. A piece of the stem of this plant that had been kept in the dark produced two roots, one above and one below, — one, therefore, opposed to the direction of the action of gravity, and the other in the direction of that action. Even in pieces of the willow, suspended in a moist atmosphere, roots develop better and over a greater length of the stem on the less illuminated side.

Although the experiments with pieces of young willow-twigs may seem to show that gravity is not a factor in regulating the development of the new parts, the results show in reality only that internal factors have a preponderating influence. By means of another series of experiments it can be shown that gravity does have an influence on the production of the new parts. It is evident that in order to test the action of gravity, pieces must be placed in different positions in relation to the vertical. It will be found, if this is done, that different results are obtained according to the angle that the piece makes with the vertical. If a piece is suspended in a moist atmosphere, with its *apical end upward*, the smaller the angle that the piece makes with the vertical so much the more are the leaf-buds that develop confined to the upper part of the piece, and so much the more do they develop from all sides of the upper end; conversely, the greater the angle with the vertical, *i.e.* the more nearly horizontal the position of the piece, so much the more are the leaf-buds that develop found along the *upper side* of the apical end (as well as around the end). If the piece is placed in a horizontal position, the leaf-buds develop not only around the apex, but they develop along the entire length of the upper surface, best, however, near the apical end.

If similar pieces are suspended in oblique positions, with the *basal end upward*, different results are obtained. In the preceding experiment the polarity of the piece and gravity act together, while in this experiment their action is opposed. Although there is a great amount of variability in the results, yet the action of gravity is found to have less influence on the result than has the inner polarity, and the influence of the latter is so much greater that the action of gravity is hardly noticeable.

The roots do not show as markedly the influence of gravity as

do the leaf-buds, yet Vöchting has found that the position in which they appear varies with the position of the piece with respect to the vertical.

In the preceding cases the rudiments of the leaf-buds and of the roots were probably present in most cases, so that gravity only awakens them into activity. In other forms, as, for instance, in
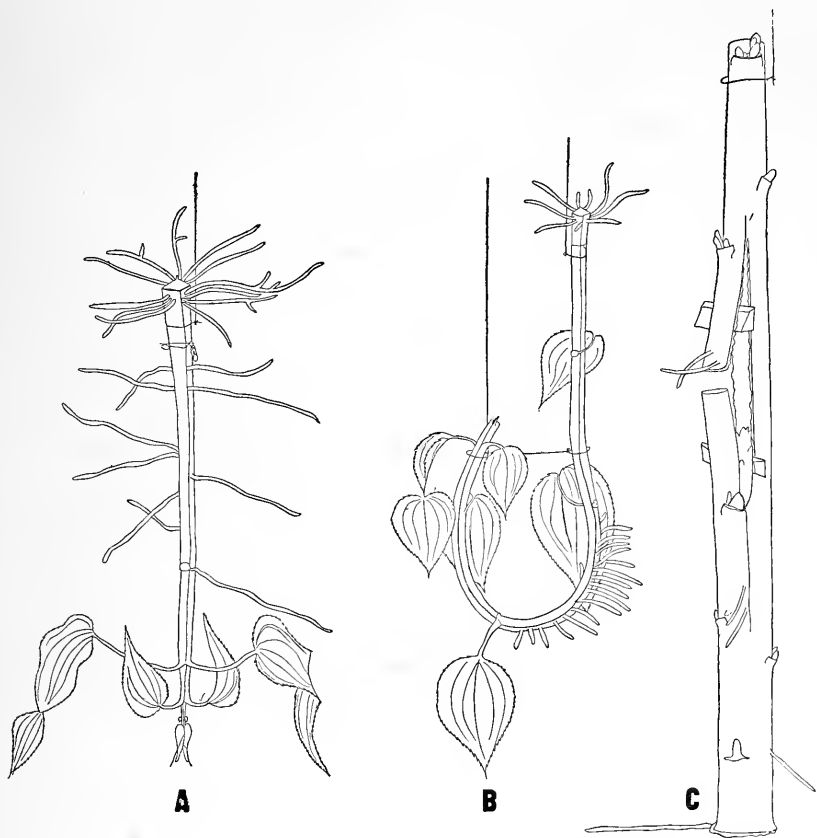


FIG. 34.—After Vöchting. *A.* End of a piece of *Heterocentron diversifolium.* Apex downward. *B.* Piece of same bent and suspended "with concave-side upward." *C.* Piece of a stem of *Salix viminalis.* Apex upward. A piece of the side has been lifted up and two wedges inserted.

heterocentron, it is possible to show that gravity may even determine the production of new buds. If pieces of the end of a branch, including the growing point, are suspended vertically, some with the apical end upward, others with the basal end upward (Fig. 34, *A*), the former produce roots only around the base, but in the latter roots appear frequently, not only at the base, but even extending along the stem. They appear not only at the nodes, where pre-

formed rudiments may be present, but also in the internodes, where there are no rudiments of roots.

Stems of heterocentron placed in a horizontal position produce a circle of roots around the base, and later, in several cases, roots from the under surface of the stem, both from the nodes and the internodes; but these roots are smaller than those at the base. Those around the base are often longer on the lower side than on the upper side.

Vöchting has also studied the regeneration of pieces of roots of the poplar and of the elm suspended horizontally in a moist chamber. A callus develops from the cambium region of the basal end, and from this a thick bunch of adventitious sprouts grows out. A weak callus may develop on the *apical end* also, from which a few roots develop. In other cases adventitious shoots are produced also from the *apical callus*, especially from the upper edge of the callus. The results are variable, but show that at times leaf-shoots may develop from the apical end of the root. It is also singular to find that, while pieces of the root produce new leaf-shoots very readily, yet they often fail to produce new roots, or produce only a few that arise from the apical callus or from the sides near that region. It is difficult to show that gravity has any influence on the result.

Vöchting recognizes another sort of influence that determines the position of new organs on a piece. If a young, growing end of a stem of *Heterocentron diversifolium* is suspended by two threads in a horizontal position, the ends bend upward as a result of the negative geotropism of the piece. The new roots appear at the base of the piece, *and also on the convex side of the bent part of the stem*, as shown in Fig. 34, *B*. The same result can be obtained by forcibly bending a twig, and then tying the ends together, so that it remains in its bent position. If a piece of this sort is suspended in a moist atmosphere, with the bent inner *concave side turned upward*, the roots appear on the base and at the bend, especially on the *under side*, both from the nodes and internodes. If now in order to see if gravity takes any part in the result the next piece is suspended with the outer *convex side* of the bent part turned *upward*, it is found that many of the pieces produce roots only at the base, but others produce roots also at the bent portion of the stem, but they are fewer than in the last experiment. The roots arise for the most part on the *under side* of the arch, and only a few arise from the upper part. It is clear that gravity is also one of the factors in the result. Leaf-buds arise in these pieces with the concave side turned *upward* only near the apex; rarely one may develop on the lower part of the basal end. In pieces with the concave side turned *downward* the leaf-buds arise for the most part at the apex, but sometimes they appear on the

upper part of the basal arm. The results are due to two factors, gravity and an inner "force" that is supposed to be the resultant of a growth phenomenon taking place in the bent portion. Vöchting supposes that a process of growth takes place as a result of the bending; "the plasma streams to this region, and a new development takes place here more easily." Vöchting adds that this view will not explain the morphological character of the new organs, and that this must be due to quite other causes. The results may, I venture to suggest, find a simpler explanation as the result of the bending, disturbing the tensions of the protoplasm, causing the two arms of the piece to act as if they had been separated from each other. This idea is more fully developed in a later chapter.

Sachs has criticised Vöchting's general conclusion in regard to the internal factors that determine the regeneration in a piece of the stem of a plant. He gives very little weight to the innate polarity of the piece, and attempts to explain the results as due to certain substances in the stem of such a sort that, accumulating in any region, they determine the kind of regeneration that takes place. Sachs also assumes that gravity acts on these substances in such a way that the root-forming substances flow downward and the shoot-forming substances flow upward. In a piece of a stem, the two formative substances contained in it accumulate at the two ends, and determine the kind of regeneration that takes place. It is evident that Sachs' hypothesis fails to explain the method of regeneration of an inverted piece suspended in a vertical position, since the roots appear at the upper end and the shoots at the lower end. Sachs explains this as the result of the previous action of gravity on the piece, while the piece was a part of the tree and stood in a vertical direction. He supposes the longer time that gravity has acted on the piece has determined its basi-apical directions, so that this influence is shown in the inverted piece, rather than the action of gravity on it in its new position. This conception involves quite a different idea from the original one of formative substances flowing in definite directions. Moreover, Vöchting has met this interpretation by using the twigs of the weeping willow, that hang downward on the tree. If gravity has acted on these drooping twigs in the way that Sachs supposes it can act, then we should expect to find, if Sachs' view is correct, that roots would develop at the apical end of a piece of the twig, and leaves at the basal end, if the piece is hung vertically with its basal end (*i.e.* the end originally nearer the trunk of the tree) upward. The regeneration of these pieces shows, however, that they behave in the same way as do pieces of twigs that have always stood vertically on the tree. There can be, therefore, no doubt that the distinction between base and apex is an expression of some innate quality of the plant itself. That an

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external factor, gravity, is also a factor in the regeneration of the pieces, is abundantly shown by the experiments of Vöchting and others, but that innate factors are also at work cannot be doubted. We find evidence in many animals of a similar difference between the two ends of a piece, and we speak of this difference between the anterior and posterior ends of a piece as its polarity. What this polarity may be we do not know, and it is even doubtful whether we should be justified in speaking of it as a force in the sense that the difference in the ends of a magnet is the result of a magnetic force. The kind of polarity shown by animals and plants does not seem to correspond to any of the so-called forces with which the physicist has to deal, but a further discussion of this question will be deferred to a later chapter.

The preceding account of regeneration in some of the higher plants has shown that their usual method of regeneration is by means of latent buds that are present along the sides of the stem, or by means of adventitious buds that develop anew along the sides of the stem. In a few cases new buds may develop from the new tissue of the callus that forms over the cut-ends, but in such cases the new shoots, or the new roots, are much smaller in diameter than the end from which they arise, and usually several or many new shoots develop on the same callus. In these respects the regeneration of the higher plants is different from that of the higher animals, for, in the latter, the new part arises from the entire cut-surface. This difference is no doubt connected with differences in the normal method of growth in plants and in animals, and an explanation of the growth would, perhaps, also give an explanation of the mode of regeneration. The normal method of growth in higher plants takes place largely by the formation of lateral buds, as well as by terminal growth, and we find that regeneration takes place in most cases from the same lateral buds or from others of a similar kind that develop after the piece has been separated.

It is sometimes stated that the higher plants do not regenerate at the cut-ends, *because* they produce buds at the sides. The statement implies that there is some sort of antagonism between the regeneration of a bud at the end, and the development of buds at the side. It may be true that the development of a latent bud at the side might suppress the tendency to produce a bud at the end, if such a tendency exists; but if we remove the lateral, pre-formed buds, new ones develop at the sides, and not at the end. That there need not be an antagonism between the formation of a bud, or of buds, at the end, and also at the sides, is shown in Vöchting's experiments with the roots of the poplar. In these, leaf-shoots and root-shoots developed both from the callus over the cut-end, and at the side of the piece also. It has further been shown that, although a piece of the internode does

not produce new leaf-buds at the sides, neither does it regenerate a new apical bud at the end.

A most interesting fact connected with the regeneration of the higher plants is, as has been pointed out, that even when a callus is formed over the cut-end, and new growth takes place from this callus,
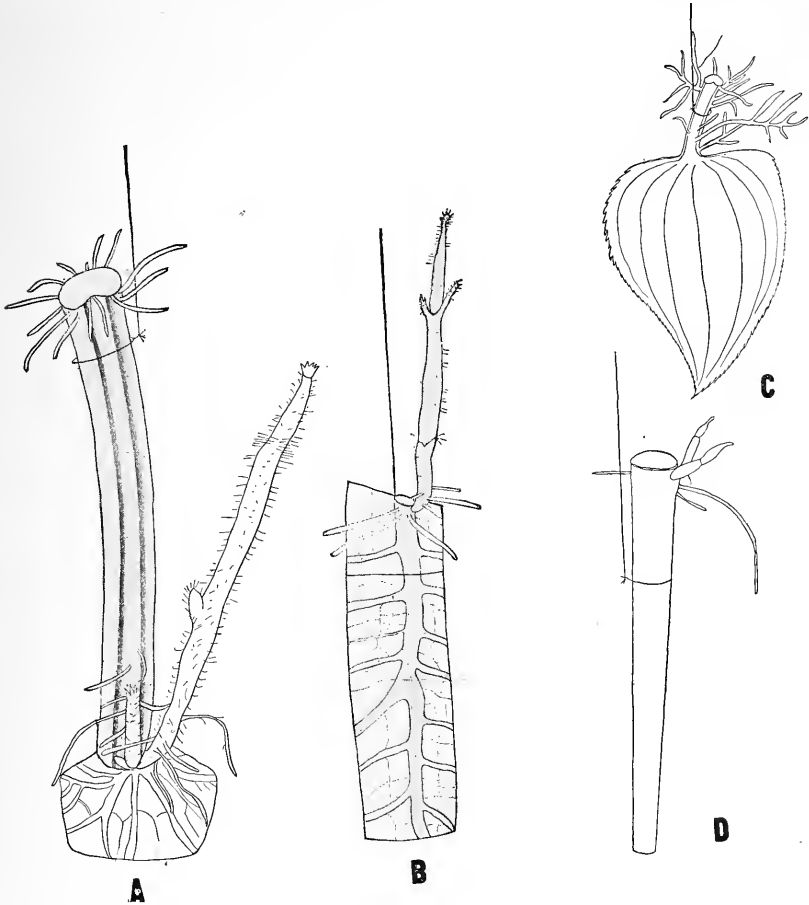


FIG. 35.—After Vöchting. *A.* Leaf-stalk of *Begonia rex* with a portion of the lamina. Suspended with base upward. *B.* Piece of lamina of leaf of same. *C.* Leaf of *Heterocentron diversifolium*. *D.* Leaf-stalk of *Begonia discolor*.

there is produced, not a single terminal bud, but a number of separate buds. The piece does not complete itself, but produces new buds, that make new branches. The explanation of this mode of regeneration in plants is not known. It appears to be connected with the production, by means of buds, of all the new structures. Why this should occur we do not know, and the only suggestion that offers

itself is that the result may be in some way connected with the hard cell walls in plants that make difficult the organization of large areas into a new whole. As a result, the new development takes place in a small group of similar cells, that are sufficiently near together to organize themselves into a whole despite the interference met with in the cell walls.

Vöchting has also studied the regeneration of pieces of the liverwort, *Lunularia vulgaris*. The results have been already partly given in the first chapter. If cross-pieces are taken from the thallus, each produces a new bud at its anterior or apical end (Fig. 9, $A$, $A^1$). The new bud arises from the cut-surface, or very near it, from a group of cells of the midrib that lies nearer the under side (Fig. 9, $A^2$). The bud gives rise to a new thallus that springs from a narrow base at its origin from the old piece. If a piece is cut longitudinally from the thallus along the old midrib, the new bud arises at the anterior end from the midrib (Fig. 9, $B$). It comes either from the anterior cut-surface near the inner edge, or from the anterior end of the inner edge, and in some cases two new buds arise, one at each of these places. If the piece is removed from one side of the midrib it does not regenerate as quickly as when a part of the midrib is present, but when the new bud develops it arises from the anterior part of the inner edge (Fig. 9, $B^1$). If the piece is cut far out at one side, it may be a long time before the new bud arises. This difference in the rate of development of these pieces is explained by Vöchting as due to the simpler character of the cells near the midrib.

If oblique pieces are cut off, with an anterior oblique cut-edge, as shown in Fig. 9, $C$, $C^1$, the new bud arises along the anterior surface. If the piece includes a portion of the old midrib at its inner end, the new bud arises from this (Fig. 9, $C$), but if the piece lies to one side of the midrib, the new bud arises near the anterior end of the anterior oblique surface (Fig. 9, $C^1$, $C^2$)        .

A number of experiments that were made in order to determine what part gravity and light may take in the regeneration gave nearly negative results. The regeneration appears to result largely from internal factors.

If a piece of the thallus is divided parallel to its surface, the two parts may each produce a new thallus, but this arises much more readily from the lower piece. If a piece of the latter is cut into small pieces no larger than half a cubic millimetre, and even much smaller, each may produce a new thallus.

Vöchting also studied the regeneration of parts having a limited growth. If a gemmiferous capsule is cut off, then split into two or four pieces, and these are placed on moist sand, it is found that new buds arise along the *basal* cut-edge. In order to show that this is

not due to the new part arising on the basal end because there is no other cut-surface, the apical part of some of the pieces was cut off. These pieces, with two free ends, produced new buds only on their basal ends.

The sexual organs of lunularia are borne on the top of erect reproductive branches having a limited growth (Fig. 9, $D$), which carry later the sporiferous branches. The branches have a stalk and a terminal disk. If pieces of the stalk are cut off they do not produce any new parts for a long time, but ultimately each produces from the basal cut-surface, or not far from the basal end, a new bud (Fig. $E^1$). If the disk is left attached to the piece, the result is the same as before (Fig. $D^1$). If a twisted part of the stalk is used, new buds may develop at the base and also *near the twisted region*, as shown in Fig. 9, $E^1$. If pieces of the stalk are stuck into the sand, some with the apical end, others with the basal end in the sand, the former produce new buds at the upper basal end, the latter produce buds on the stalk just above the surface of the sand. Pieces that retain the old disk when stuck into the sand (Fig. 9, $D$) produce one or more buds along the stalk above the sand, often some distance above it. The part buried in the sand does not seem able to develop new buds, and as a result they are produced at the first region of the basal part of the stalk, where the conditions make it possible for buds to develop.

If the disk is cut entirely from the stalk and placed on moist sand, it produces adventitious buds in the region at which the stalk was removed. Buds are also produced at the bases of the rays that go off from the disk. They arise from the under side of the rays without regard to the position of the disk, *i.e.*, whether it is turned upward or downward. If the rays are cut off they produce new buds at the base (Fig. 9, $F$), and if the outer tip of the ray is also cut off, the new bud still arises at the base, as shown in Fig. 9, $F^1$. These results on pieces with limited growth agree in every respect with those that have been obtained in flowering plants. Vöchting thinks that the phenomenon is due in all cases to the limited growth of the parts. Goebel rejects this interpretation, and thinks that the results can be accounted for by the direction of the movement of formative or, at least, of building material. In favor of this view, he points out that in other liverworts the polarity is not shown in the same degree as in lunularia (according to Schostakowitsch), and also that in very old pieces of marchantia, as Vöchting has shown, the polarity disappears. In the latter case the attractive action at the vegetative point, to which the building stuff is supposed to flow, is less strong; and in longer pieces the influence of the apical region may not extend throughout the entire length of the thallus. In favor

of this interpretation he points out that in young prothallia of os-
munda, adventitious shoots do not appear, but in older plants, that
have become longer, these shoots may appear at the base, because
this region is no longer influenced by the apex, and consequently it
is possible for building material to accumulate at the basal end.
It may be granted that Goebel's idea is possibly correct, viz. that the
apex, or the apical end of a piece, may have some influence in pre-
venting the development of shoots at the base, but it does not follow
that this influence can be accounted for on the ground of a with-
drawal of building stuff from the basal part.   As I shall attempt to
show in a later chapter, this influence may be of a different nature.

It has been found by Pringsheim and others that pieces of the
stem of mosses may also produce new plants, and this holds even for
pieces of the stalk of the sporophore and of the wall of the spore
capsule (Fig. 10, *A–D*).   In this case, however, there is not produced
a new moss plant directly from the end of the piece, but threads or
protonemata grow out, as shown in Fig. 10, *A*, *B*, and from these
new moss plants are formed in the same way as on the ordinary
protonema.   The threads that arise from the piece grow out from
single cells in the middle part of the stem.   These cells are less dif-
ferentiated and are richer in protoplasm than are the other cells in
the stem.

The prothallia of certain ferns are said by Goebel to regenerate if
cut in two ; at least this is true for the part that contains the vegeta-
tive point.   In a piece without the growing point, the cells are very
little specialized, and the piece may remain alive ; yet it is incapable
of producing a new growing point.   Comparing this result with the
power of regeneration possessed by lower animals, Goebel states [1] that
since in a plant new organs may arise without the typical form of the
plant being produced, "therefore, the completion of a leaf, for instance,
that has been injured, would *be of no use* to the plant, while in ani-
mals that do not have a vegetative point, the loss of an organ is a
permanent disadvantage in case the organ removed cannot be regen-
erated."   The "explanation" of the difference in the two cases is
supposed, apparently, by Goebel, to depend on the usefulness, or
non-usefulness, of the regenerative act !

Brefeld has described several cases of regeneration in moulds.
There is produced from the zygospore of *Mucor mucedo* a germinat-
ing tube that forms at its end a single sporangium.   If the tube is
destroyed or injured, a second one is formed from the zygospore, and
if this is injured a third time, a new tube is produced.   Each time
the sporangium is smaller than in the preceding case.

If the spore-bearing stalk of *Coprinus stercorarius* is cut off, the

[1] Goebel, '98, page 37.

end grows out and produces a new sporangium. If pieces of the stem are cut off and placed in a nourishing medium, they produce from the ends a new mycelium, and from this new erect hyphæ may develop. In the former case, the cut-end regenerates the part removed in somewhat the same way that an animal regenerates at the cut-end; in the latter, there is a return to the mycelium stage, as in
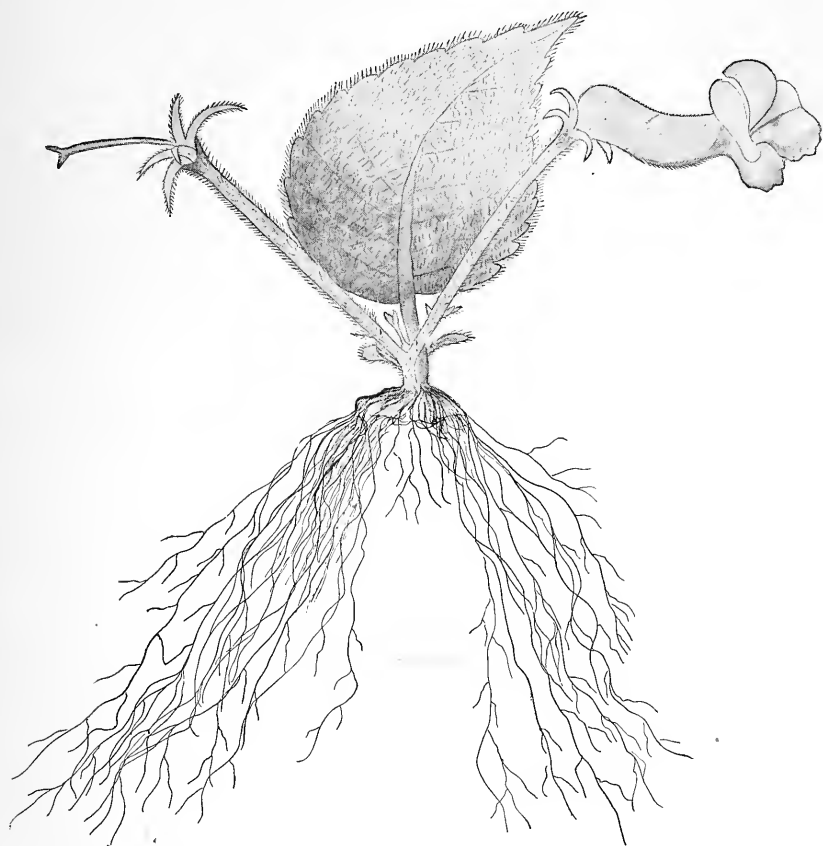


FIG. 36. — After Goebel. *Achimenes Haageana.* A leaf-cutting of a plant in flower. The new plant, regenerating at base of leaf-stalk, proceeded at once to produce a flower.

the piece of the moss that produces a new protonema. If the my-celium and the protonema are looked upon as an embryonic stage in the formation of the sexual form, there is a return in these cases to an embryonic form or mode of development.

One of the most remarkable and important discoveries in con-nection with the regeneration of plants is that the new individuals that develop from leaves cut off from certain plants differ according to

the region of the old plant from which the leaf has been taken. Sachs discovered in 1893 that when the leaves of the begonia are taken from a plant in bloom, the adventitious buds that develop from the leaves very quickly produce new flowers. If the leaves are taken from a plant that has not yet produced flowers, the new plant that develops from the leaf does not produce flowers until after a much longer time. Goebel repeated the experiment with achimenes, and found that the new plants that develop from leaves from the flowering part of the stem (Fig. 36) produce flowers sooner than do the plants that develop from leaves from the base of the same plant. The former produce, as a rule, only one or two leaves and the flower stalk; the latter, a large number of leaves.

Sachs explains these results as due to a flower-forming stuff that is supposed to be present in the leaves when the plant is about to blossom. This material is supposed to act on the new plant that develops from the leaves, and to bring it sooner to maturity. Goebel points out that the result may also be explained by the fact that the leaves in the flowering region may be poorer in food materials and, in consequence, the adventitious buds that they produce are weaker, and, as experience has shown in other cases, a weakening of the tissues brings about more quickly the formation of flowers. Nevertheless, Goebel inclines to Sachs' hypothesis of specific or formative stuffs, without, however, denying that there is also an inner polarity or "disposition" that also appears in the phenomena of regeneration. But Goebel seems to think that the phenomena of polarity "can most easily be brought under a common point of view by means of Sachs' assumption that there are different kinds of stuffs that go to make the different organs. In the normal life of the plant shoot-forming stuffs are carried to the vegetative points, while root-forming materials go to the growing ends of the roots. In consequence, when a piece is cut off and the flow of the formative stuffs is interrupted, the root-forming stuff will accumulate at the base of the piece and the shoot-forming stuffs at the apex. In the leaf the flow of all formative substances is toward the base of the leaf, and it is in this region that the new plants arise after the removal of the leaf." A confirmation of this point of view, Goebel believes, is furnished by the following cases. Some monocotyledonous plants seldom set seed because the vegetative organs, the bulbs, tubers, etc., that reproduce the plant, exert a stronger attraction upon the building stuff than do the young seeds.[1] Lindenmuth has shown in some of these forms that pieces of the stem produce, near the base, numerous bulblets, because the building stuff moves toward the base. In *Hyacinthus orientalis*, on the other hand, bulblets are produced at

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[1] Examples of this are found in *Lilium candidum, Lachenalia luteola.*

the apical part of a piece of the flowering plant. In this plant the seeds ripen normally, presumably because of the migration of stuffs toward the developing seeds. The results in all these cases are due, Goebel thinks, to the direction of the flow of formative stuffs, and cannot be explained as connected in any way with the limited growth of the part.

These cases, cited by Goebel, are not in my opinion altogether to the point; and they fail also to establish convincingly the conclusion that Goebel draws from them. It may be granted that starch is stored up in certain parts of the plant, and if these parts are removed the starch may be stored up in other parts, as Vöchting ('87) has shown; but that the movement of this starch to the base can account for the lack of development of the seeds in certain cases seems to me improbable, or, at least, far from being established by the cases cited. It may be granted that the presence of starch in a region may act on the organs there present and determine their fate. Vöchting has shown in the potato that by removing the tubers the axial buds, especially in the basal leaves, become tuber-like bodies, but it should not be overlooked that the tubers themselves are formed from underground stolons, that arise in the same way as do those in the axils of the leaves. It would be erroneous, I think, to conclude from these cases of the effect of food stuffs on certain regions that there are formative stuffs for all the organs of the plant, and that these stuffs migrate in different directions and determine the nature of the part. Even the migration of such substances *in definite directions in the tissue* is itself in need of explanation, since it has been made highly probable by Vöchting's experiments that this is not produced by agents outside of the plant. Furthermore, Vöchting has shown that the tendency of starch to accumulate in the tubers and the formation of the tuber are separate phenomena.

This hypothesis of formative stuffs held by such able botanists as Sachs and Goebel demands nevertheless serious consideration, if for no other reason than that if it is true it offers quite a simple explanation of many phenomena of growth and of regeneration. We should, I think, distinguish between specific or formative stuffs and building or food stuffs. By specific stuffs is meant a special kind of substance which, being present in a part, determines the nature of the part. Sachs supposes, for instance, that a specific substance is made by the leaves of a plant which is transported to the vegetative, growing region (which has so far produced only leaves), and changes its growth so that flowers are produced. Goebel does not commit himself altogether to specific stuffs of this sort, but speaks also of building stuffs. By building stuff we may understand food material that is necessary for growth, and from which any part of the plant

may be made. Its presence in larger or smaller quantities may determine what a particular part shall become, but further than this it exerts no specific action. This means that the presence of a certain amount of food substance may determine what a given region shall produce, but it is not supposed that there are different kinds of food materials that correspond to each kind of structure. If there were such, they would not differ from specific substances, unless we wish to make subtle distinctions without any basis of fact to go upon.

Goebel points out that there is evidence to show that the greater or less quantity of food substance contained in a plant often determines the nature of its growth, as for instance the production of flowers when the food supply runs low and the production of foliage when the food supply is abundant. This difference may explain Sachs' experiment with begonia leaves; and if so, there is no need for supposing specific flower stuffs to be made in the plant.

There is another point of view which has been, I think, too much neglected, viz. that the production of food stuffs is itself an expression of changes taking place in the living tissues, and if the structure is changed so that it no longer produces the same substances it may then lead to the development of different kinds of organs. The difference in the regeneration of an apical and a basal leaf of begonia may be due to some difference in the structure of the protoplasm. The greater or smaller amount of starch produced in these leaves may be only a measure of, and not a factor in, the result.

In this same connection another question needs to be discussed. It is assumed by several botanists that in a normal plant the latent shoots or buds along the stem do not develop so long as the terminal shoots are growing, because the latter use up all the food material that is carried to that region. If the terminal bud is destroyed the lateral shoots then burst forth, in consequence, it is assumed, of the excess of food stuff that now comes to them. I do not believe that the phenomena can be so easily explained. If a piece of a plant is cut off, the leaves removed, and the piece suspended in a moist chamber and kept *in the dark*, the lateral buds at the apex will begin to develop. If we assume that the piece cannot develop any new food substance in the dark, then it contains just the same amount as it did while a part of the plant, and yet that amount is ample for the development of the lateral buds. Moreover, only the more apical buds develop; but if the piece is then cut in two, the apical buds of the basal piece, that had remained undeveloped, will now develop. How can this be explained by the amount of food substances in the piece ? If it is assumed that in the normal plant the food substances flow only to the growing points, and the buds are out of the main current and fail in consequence to develop, it can be shown that this

idea also fails to explain certain results. Vöchting has found, for example, that if an incision is made *below* a bud and the piece containing the bud be lifted up somewhat from the rest of the piece, remaining attached only at its anterior end, the bud will begin to develop. In this case the conditions preclude an accumulation of food substances in the piece, and the bud is even farther removed than at first from the main current, yet it begins to develop.

We shall find, I think, that the idea of food stuffs fails to explain some of the simplest phenomena, and while it need not be denied that under certain conditions the presence or accumulation of food materials may produce certain definite results, yet such food stuffs seem to play a very subordinate part as compared with certain other internal or innate factors.

# CHAPTER V

## REGENERATION AND LIABILITY TO INJURY

THERE is a widespread belief amongst zoologists that a definite relation exists between the liability of an animal to injury and its power of regeneration. It is also supposed that those individual parts of an animal that are more exposed to accidental injury, or to the attacks of enemies, are the parts in which regeneration is best developed, and conversely, that those parts of the body that are rarely or never injured do not possess the power of regeneration.

Not only do we find this belief implied in many ways, but we find this point of view definitely taken by several eminent writers, and in some cases carried so far that the process of regeneration itself is supposed to be accounted for by the liability of the parts to injury. In order that it may not appear that I have exaggerated the widespread occurrence of this belief, a few examples may be cited.

Réaumur in 1742 pointed out that regeneration is especially characteristic of those animals whose body is liable to be broken, or, as in the earthworm, subject to the attacks of enemies. Bonnet (1745) thought that such a connection exists as has just been stated, and that the animals that possess the power of regeneration have been endowed with germs set aside for this very purpose. He further believed that there would be in each animal that regenerates as many of these germs as the number of times that it is liable to be injured during its natural life. Darwin in his book on *Animals and Plants under Domestication* says: "In the case of those animals that may be bisected, or chopped into pieces, and of which every fragment will reproduce the whole, the power of regrowth must be diffused throughout the whole body. Nevertheless, there seems to be much truth in the view maintained by Professor Lessona[1] that this capacity is generally a localized and special one serving to replace parts which are eminently liable to be lost in each particular animal. The most strik-

[1] Delage and Giard give Lessona ('69) the credit for first stating that the phenomenon of regeneration is an adaptation to liability to injury; but Réaumur first suggested this idea in 1742, and Bonnet in 1745. Delage's interpretation, viz. that Lessona ascribed this to a *prévoyance de la nature*, has been denied by Lessona's biographer, Camerano (*La Vita di M. Lessona, Acad. R. d. Torino*, 2, XLV, 1896), and by Giard (*Sur L'autotomie Parasitaire*, etc., *Compt. Rendus de Séances de la Société de Biologie*, May, 1897).

ing case in favor of this view is that the terrestrial salamander, according to Lessona, cannot reproduce lost parts, whilst another species of the same genus, the aquatic salamander, has extraordinary powers of regrowth, as we have just seen; and this animal is eminently liable to have its limbs, tail, eyes, and jaws bitten off by other tritons."

Lang, referring to the brittleness of the tails of lizards, points out that this is a very useful character, since the bird of prey that has struck at a lizard gets hold of only the last part of the animal to disappear under cover; the lizard escapes by breaking off its tail. The brittleness of the tail is, therefore, an adaptive character that has become fixed by long inheritance.

To this example may be added that of certain land snails in the Philippine Islands. The individuals of the genus helicarion live on trees in damp forests, often in great droves. They are very active, and creep with unusual swiftness over the stems and leaves of the trees. Semper has recorded that all the species observed by him have the remarkable power of breaking off the tail (foot) close behind the shell, if the tail is roughly grasped. A convulsive movement is made until the tail comes off, and the snail drops to the ground, where it is concealed by the leaves. Semper adds that in this way the snails often escaped from him and from his collectors, leaving nothing behind but their tails. The tail is said to be the most obvious part of the animal, and it is assumed that this is, therefore, the part that a reptile or bird would first attack.[1] Lang states that in this case external influences have produced an extraordinarily well-developed sensitiveness in the animal, so that it reacts to the external stimulus by voluntarily throwing off the tail. It would be, of course, of small advantage to be able to throw off the tail unless the power of regenerating the lost organ existed, or was acquired at the same time as the extreme sensitiveness that brings about the reaction. Lang does not state, however, explicitly that he believes the regenerative power to have arisen through the exposure of the tail of the lizard and the tail of the snail to injury, although he thinks that the mechanism by means of which these parts are thrown off has been acquired in this way. Several other writers have, however, used these same cases to illustrate the supposed principle of liability to injury and power of regeneration.

Weismann in his book on *The Germ Plasm* has adopted the principle of a connection between regeneration and liability to injury and has carried it much farther than other writers. We can, therefore, most profitably make a careful examination of Weismann's

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[1] Whether, having once failed in this way to obtain the snail, the bird or lizard would not learn to make a frontal attack is not stated. Or shall we assume that the tail is all that is wanted?

position.    His general idea may be gathered from the following
quotation: [1]  " The dissimilarity, moreover, as regards the power of
regeneration *in various members of the same species,* also indicates that
adaptation is an important factor in the process.    In proteus, which in
other respects possesses so slight a capacity for regeneration, the gills
grow again rapidly when they have been cut off.    In lizards again this
power is confined to the tail, and the limbs cannot become restored.
In these animals, however, the tail is obviously far more likely to
become mutilated than are the limbs, which, as a matter of fact, are
seldom lost, although individuals with stumps of legs are occasionally
met with.    The physiological importance of the tail of a  lizard con-
sists in the fact that it preserves the animal from total destruction, for
pursuers will generally aim at the  long trailing tail, [2] and thus the
animal often escapes, as the tail breaks off when it is firmly seized.
It is, in fact, as Leydig was the first to point out, specially adapted for
breaking off, the bodies of the caudal vertebræ from the seventh
onward being provided with a special plane of fracture so that they
easily break  into two transversely.    Now if this capability of fracture
is provided for by a special arrangement and modification of the parts
of the tail, we shall not be making too daring an inference if we
regard the regenerative power of the tail as *a special adaptation, pro-*
*duced by selection, of this particular part of the body, the frequent loss*
*of which is in a certain measure provided for,* and not as the outcome
of an unknown ' regenerative power ' possessed by the entire animal.
This arrangement would not have been provided if the part had been
of no, or of only slight, physiological importance, as is the case in
snakes and chelonians, although these animals are as highly organized
as lizards.    The reason that the limbs of lizards are not replaced is, I
believe, due to the fact that these animals are seldom seized by the
leg, owing to their extremely rapid movements."    Overlooking the
numerous cases of the regeneration of internal organs that have been
known for several years, and basing his conclusion on a small, uncon-
vincing experiment of his own on the lungs of a few salamanders,
Weismann concludes : " Hence there is no such thing as a general
power of regeneration ;  in each kind of animal this power is graduated
according to the need of regeneration in the part under consideration ;
that is to say, the degree in which it is present is mainly in proportion
to the liability of the part to injury."

    After arriving at this conclusion the following admission is a
decided anticlimax : " The question, however, arises as to whether
the capacity of each part for regeneration results from special process
of adaptation, or whether regeneration occurs as the mere outcome —

[1] *The Germ Plasm.*    Translation by W. Newton Parker, 1893, page 116.
[2] There are no facts that show that this statement is not entirely imaginary.   T. H. M.

which is to some extent unforeseen — of the physical nature of an animal. Some statements which have been made on this subject seem hardly to admit of any but the latter explanation." After showing that some newts confined in aquaria attacked each other, "and several times one of them seized another by the lower jaw, and tugged and bit at it so violently that *it would have been torn off had I not separated the animals*," [1] and after referring to the regeneration of the stork's beak, Weismann concludes: "Such cases, the accuracy of which can scarcely be doubted, indicate that the capacity for regeneration does not depend only on the special adaptation of a particular organ, but that a general power also exists which belongs to the whole organism, and to a certain extent affects many and perhaps even all parts. By virtue of this power, moreover, simple organs can be replaced when they are not specially adapted for regeneration." The perplexity of the reader, as a result of this temporary vacillation on Weismann's part, is hardly set straight by the general conclusion that follows on the same page : "We are, therefore, led to infer that the general capacity of all parts for regeneration may have been acquired by selection in the lower and simpler forms, and that it gradually decreased in the course of phylogeny in correspondence with the increase in complexity of organization ; but that it may, on the other hand, be increased by special selective processes in each stage of its degeneration, in the case of certain parts which are physiologically important and are at the same time frequently exposed to loss."

There are certain statements of facts in the same chapter that are incorrect, and the argument is so loose and vague that it is difficult to tell just what is really meant. As a misstatement of fact I may select the following case : It is stated that lumbriculus does not have the power of regenerating laterally if cut in two, and it is argued that a small animal of this form could rarely be injured at the side without cutting the animal completely in two. As a matter of fact, lumbriculus can regenerate laterally, and very perfectly, as any one can verify if he takes the trouble to perform the experiment ; but, of course, if the whole animal is split in two lengthwise the pieces die, or if a very long piece is split from one side the remaining piece usually disintegrates. If, however, the anterior end is split in two for a short distance, or if a piece is partially split in two, the half remaining in contact with the rest of the piece completes itself laterally. The same result follows also in the earthworm.

As an example of looseness of expression I may quote the following from Weismann : "A useless or almost useless rudimentary part may often be injured or torn off *without causing processes of selection to occur which would produce in it a capacity for regeneration*. The

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[1] The *italics* are, of course, my own. T. H. M.

tail of a lizard again, which is very liable to injury, becomes regenerated because, as we have seen, it is of great importance to the individual and if lost its owner is placed at a disadvantage." And as an example of vagueness, the following statement commends itself: " Finally the complexity of the individual parts constitutes the third factor which is concerned in regulating the regenerative power of the part in question ; for the more complex the structure is, the longer and the more energetically the process of selection must act in order to provide the mechanism of regeneration, which consists in the equipment of a large number of different kinds of cells with the supplementary determinants which are accurately graduated and regulated as regards their power of multiplication."

Without attempting to disentangle the ideas that are involved in these sentences, let us rather attempt to get a general conception of Weismann's views. In a later paper (1900), in reply to certain criticisms, he has stated his position somewhat more lucidly. In the following statement I have tried to give the essential part of his hypotheses : Weismann believes the process of regeneration to be regulated by "natural selection " ; in fact, he states that it has arisen through such a process in the lower animals — since they are more subject to injury — and that it has been lost in the higher forms except where, on account of injury, it has been retained in certain parts. Thus when Weismann speaks of regeneration as being an adaptation of the organism to its environment, we must understand him to mean that this adaptation is the result of the action of natural selection. We should be on our guard not to be misled by the statement that because regeneration is useful to the animal, it has been acquired by natural selection, since it is possible that regeneration might be more or less useful without in any way involving the idea that natural selection is the originator of this or of any other adaptation. It will be seen, therefore, that in order to meet Weismann on his own ground it will be necessary to have a clear understanding in regard to the relation of regeneration to Darwin's principle of natural selection. With Weismann's special hypothesis of the " mechanism," so-called, by which regeneration is made possible we have here nothing to do, but may consider it on its own merits in another chapter.

In order to have before us the material for a discussion of the possible influence of natural selection on regeneration, let us first examine the facts that bear on the question of the liability of the parts to injury and their power to regenerate, and in this connection the questions concerning the renewal of parts that are thrown off by the animals themselves in response to an external stimulus are worthy of careful consideration. A comparison between the regeneration of these parts with that of other parts of the same animal gives also

important data. Furthermore, a comparison may be made between different parts of the same animal, or between the same parts of different animals living under similar or dissimilar conditions.

There are only a few cases known in which a systematic examination has been carried out of the power of regeneration of the different parts of the body of the same animal. Spallanzani's results show that those salamanders that can regenerate their fore legs can regenerate their hind legs also. Towle, who has examined in my laboratory the regeneration of a number of American newts and salamanders, finds also that both the fore and hind legs regenerate in the same forms. The tail and the external gills, in those newts with gills, also regenerate. It has also been shown in triton that the eye regenerates if a portion of the bulb is left. Broussonet first showed (1786) that the fins of fish have the power to regenerate, although, strangely enough, Fraisse and Weismann state that very little power of regeneration is present in the fins of fish. I have found that the fins of several kinds of fish regenerate, belonging to widely different families.[1] In *Fundulus heteroclitus* I have found that the pectoral, pelvic, caudal, anal, and dorsal fins have the power of regeneration. In reptiles the feet do not regenerate, — at least no cases are known, — but the tail of lizards has this power well developed. In birds neither the wings nor the feet regenerate, but Fraisse has described the case of a stork in which, the lower jaw being broken off, and the upper being cut off at the same level, both regenerated. Bordage has recorded the regeneration of the beak of the domesticated fighting cocks (of the Malay breed) of Mauritius. In the mammals neither the legs, nor the tail, nor the jaws regenerate, although several of the internal organs, as described in the next chapter, have extensive powers of regeneration.

The best opportunity to examine the regenerative power in similar organs of the same animal is found in forms like the crustacea, myriapods, and insects, in which external appendages are repeated in each or many segments of the body. In decapod crustacea, including shrimps, lobsters, crayfish, crabs, hermit-crabs, etc., regeneration takes place in the walking legs of all the forms that have been examined, and this includes members of many genera and families. I have made an examination of the regeneration of the appendages (Fig. 37) of the hermit-crab. In this animal, which lives in an appropriated snail's shell, only the anterior part of the body projects from the shell. The part that protrudes is covered by a hard cuticle, while the part of the body covered by the shell is quite soft. Three pairs of legs are protruded from the shell. The first pair with large claws

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[1] *Fundulus heteroclitus, Stenopus chrysops, Decapterus macrella, Menticirrhus macrella, Carassius auratus, Phoxinus funduloides, Noturus sp.,* and a few others.

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are used for procuring food, and as organs of offence and defence; the second and third pairs are used for walking. The following two pairs, that correspond to the last two pairs of walking legs of crabs and crayfishes, are small, and are used by the animal in bracing itself against the shell. The first three pairs of legs have an arrange-
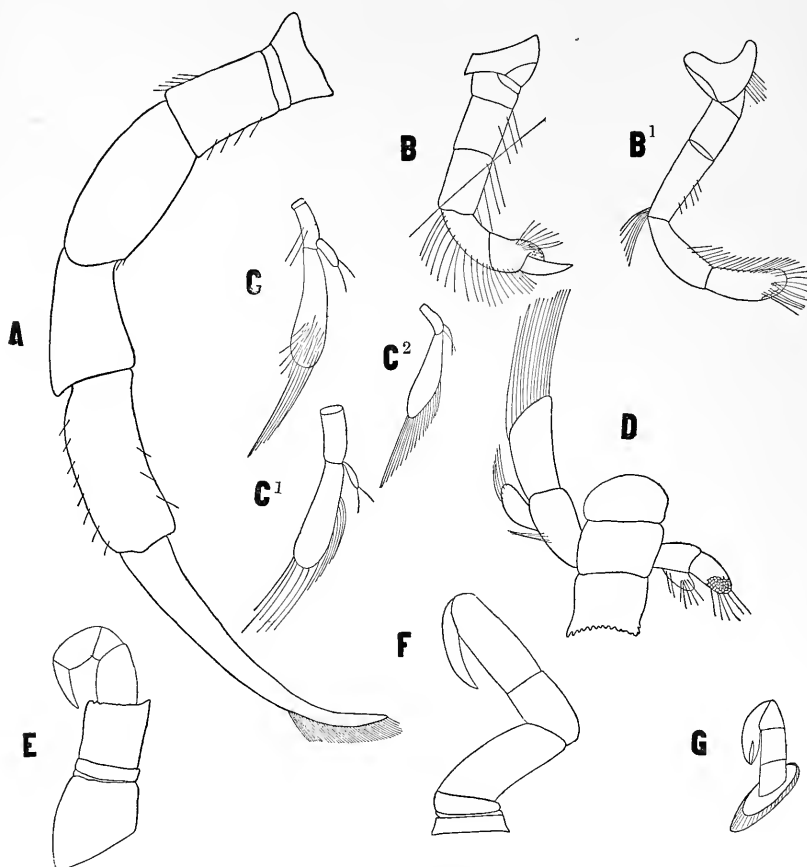


FIG. 37. — Appendages of Hermit-crab (*Eupagurus longicarpus*). *A*. Third walking leg. *B*. Next to last thoracic leg. *B*[1]. Last thoracic leg. *C*, *C*[1], *C*[2]. Three abdominal appendages of male. *D*. Telson and sixth segment with last pair of abdominal appendages. *E*. Regeneration of new leg from cut-end outside of "breaking-joint." *F*. Leg regenerating from cut made inside of "breaking-joint." *G*. Leg regenerating from cut made very near the body.

ment at the base, the "breaking-joint," by means of which the leg is thrown off, if injured. The last two pairs of thoracic legs cannot be thrown off. The first three pairs of legs are often lost under natural conditions. In an examination of 188 individuals I found that 21 (or 11 per cent) had lost one or more legs. If one of the first three legs is injured, except in the outer segment, it is thrown off at the break-

ing-joint, and a new leg regenerates from the broken-off end of the stump that is left. The new leg does not become full size, and is of little use until the crab has moulted at least once. The leg breaks off so close to the body, and the part inside of the breaking-joint is so well protected by the bases of the other legs, that it is scarcely possible that the leg could be torn off inside of the breaking-joint, and, as a matter of observation, all crabs that are found regenerating their legs under natural conditions do so from the breaking-joint. If, however, by means of small scissors, the leg is cut off quite near the body, a new leg regenerates from the cut-end, even when the leg is cut off at its very base. The breaking-joint would thoroughly protect from injury the part of the leg that lies nearer to the body, and yet from this inner part a new leg is regenerated. Moreover, the new leg is perfect in every respect, even to the formation of a new breaking-joint. In this case we have a demonstration that there need be no connection between the liability of a part to injury and its power of regeneration.

In still another way the same thing may be shown. If the crab is anæsthetized, and a leg cut off outside of the breaking-joint, it is not, at the time, thrown off — the nervous system, through whose action the breaking off takes place, being temporarily thrown out of order. After recovery, although the leg is thrown off in a large number of cases, it is sometimes retained. In such cases it is found that from the cut-end the missing part is regenerated. In this case also we find that regeneration takes place from a part of the leg that can never regenerate under natural circumstances.

The third and fourth legs of the hermit-crab cannot be thrown off, but they have the power of regeneration at any level at which they may be cut off. They are in a position where they can seldom be injured, and I have never found them absent or injured in crabs caught in their natural environment. The soft abdomen is protected by the snail's shell. At the end of the abdomen the last pair of abdominal appendages serve as anchors to hold the crab in the shell. These appendages are large and very hard, and can seldom be injured unless the abdomen itself is broken, and under these circumstances the crab dies. Yet if these appendages are cut off they regenerate perfectly, and after a single moult cannot be distinguished from normal ones.

The more anterior abdominal appendages are present only on one side of the adult, although they are present on both sides of the larva, and, to judge from a comparison with other crustacea, these appendages have degenerated completely on one side, and have become rudimentary in the male, even on the side on which they are present. They too will regenerate if they are cut off. In the female these

appendages are used to carry the eggs, and are, therefore, of use. They also have a similar power of regeneration. The maxillæ and maxillipeds of the hermit-crab have likewise the power of regeneration, as have also the two pairs of antennæ and the eyes.

In other decapod crustacea also it has been shown that the power of regeneration of the appendages is well developed. It has been long known that the crayfish and the lobster can regenerate lost parts. The first pair of legs, or chelæ, in these forms has a breaking-joint, at which the leg can be thrown off, yet in the crayfish I have seen that if the leg is cut off inside of the breaking-joint it will regenerate. The four pairs of walking legs do not possess a breaking-joint, but may be thrown off in some cases at a corresponding level. They regenerate from this level, as well as nearer the body and farther beyond this region. Przibram has recently shown that, in a number of crustacea, regeneration of the appendages takes place, even when the entire leg is extirpated as completely as possible.

Newport has shown that the myriapods can regenerate their legs, and it is known that several forms have the power of breaking off their legs in a definite region at the base if the legs are injured, and I have observed in *Cermatia forceps* that this takes place even when the animal is thrown into a killing fluid. Newport ('44) has also shown that when the legs of a caterpillar are cut off new ones regenerate during the pupa stage. It has been long known [1] that the legs of mantis can regenerate, and Bordage, who has recently examined the question more fully, has shown that a breaking-joint is present at the base of the leg. The tarsus of the cockroach also regenerates, producing only four, instead of the five, characteristic segments.[2]

A number of writers have recorded the regeneration of the legs of spiders.[3] Schultz, who has recently examined more thoroughly the regeneration of the legs in some spiders, finds that the leg is renewed if cut off at any level. He removed the leg most often at the metatarsus, but also at the tibia, and generally between two joints. In some cases the leg was cut off at the coxa, at which level it is generally found to be lost under natural conditions. Wagner observed in tarantula that when the leg is removed at any other place than at the coxa, the animal brings the wounded leg to its jaws, and bites it off down to the coxa. In the *Epeiridæ*, that Schultz chiefly made use of, this never happened. He observed, however, even in these forms, that when the leg is cut off at the coxa it regenerates better than

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[1] See Newport and Scudder.

[2] Brindley, '97.

[3] Lepelletur, *Nouveau Bulletin de la Société philomatique*, 1813, Tome III, page 254 ; Heineken, *Zool. Journal*, 1828, Vol. IV, page 284 (also for insects, *ibid.*, page 294) ; Müller, *Manual de Physiol.*, Tome I, page 30 ; Wagner, W., *Bull. Soc. Imp. Natural.*, Moscow, '87.

when cut off at any other level. Schultz states that we see here an excellent example of how regeneration is influenced by natural selection, since regeneration takes place best where the leg is most often broken off. On the other hand, the author hastens to add that since regeneration also takes place when the leg is cut off at any other
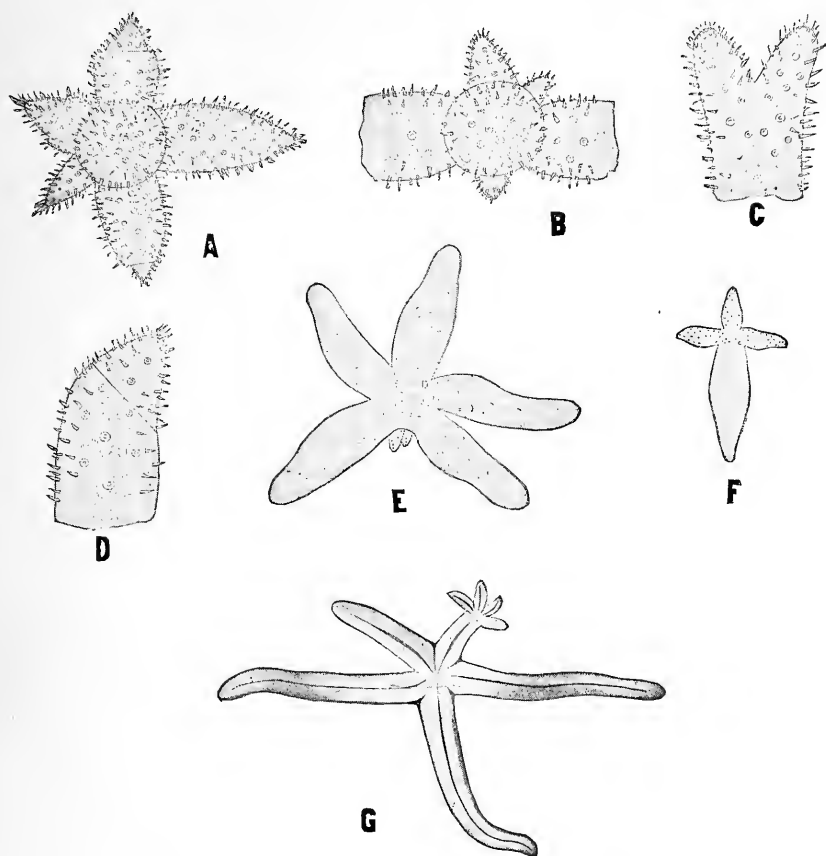


FIG. 38.— *A–F*. After King. *A*. Starfish with four arms regenerating at different levels. *B*. Three arms regenerating from disk. *C*. Arm split in two producing two arms. *D*. Arm cut off obliquely, regenerating at right angles to cut-surface. *E*. Starfish split between two arms, producing two new arms from split. *F*. An arm, with a small piece of disk attached, regenerating three new arms. *G*. After P. and F. Sarasin. Starfish (*Linckia multiformis*) with four new arms springing from end of one arm. Interpreted as a new starfish, but probably only multiple arms (see *C*, above).

level, this shows that the power to regenerate is characteristic of all parts of the organism, and is not *merely* a phenomenon of adaptation, as Weismann believes. It seems highly improbable that a spider could ever lose a leg in the middle of a segment, *i.e.* between two joints, since the segments are hard and strong and the joints much

weaker; but nevertheless the leg has the power to regenerate also from the middle of the segment, if cut off in this region.

The formation of the new part takes place somewhat differently, according to Schultz, when the leg is amputated between two segments than when cut off at the coxa. In the latter case, there is produced from the cut-end of the last segment a solid rod which, as it grows longer, bends on itself several times. Joints appear in the rod, beginning at the base. The leg is set free at the next moult. If the leg is cut off nearer the distal end a smaller rod is formed, that extends straight forward, or may be thrown into a series of folds. It lies, however, inside of the last segment, since the surface exposed by the cut is quickly covered over by a chitinous covering. The piece is set free at the next moult.

Loeb has found that if the body of the pycnogonid, *Phoxichilidium maxillare*, is cut in two there regenerates from the posterior end of the anterior half a new body-like outgrowth.

Without attempting to describe the many cases in worms and mollusks in which there is no obvious connection between the power of the part to regenerate and its liability to injury, but where it is more difficult to show that it may not exist, let us pass to an examination of the regeneration of the starfish. It has been known since the time of Réaumur that starfish have the power of regenerating new arms if the old ones are lost. It has been stated that in certain starfishes an arm itself can produce a new starfish, — Haeckel ('78), P. and R. Sarasin ('88), von Martens ('84), and Sars ('75, — but this has been denied by other observers. In several species of starfishes, the separated arm does not regenerate ; but if a portion, even a small piece, of the disk is left with the arm, a new disk and arms may develop (Fig. 38, *F*). When the arm of *Asterias vulgaris* is injured it pinches off in many cases at its base, and a new arm grows out from the short stump that remains. When these starfishes regenerate new arms in their natural environment, the new arms almost always arise from this breaking region.[1] Thus King found out of 1914 individuals of *Asterias vulgaris* collected at random, 206, or 10.7 per cent, had one or more new arms, and all these except one arose from near the disk. In other species it appears that the outer portions of the arm may be broken off without the rest of the arm being

[1] The Sarasins have described several cases in *Linckia multiformis* in which an old arm has one or more new arms arising from it. In one case (copied in our Fig. 38, *G*), four rays arise from the end of one arm, producing the appearance of a new starfish. In fact the Sarasins interpret the result in this way, although they state that there is no madreporite on the upper surface, and they did not determine whether a mouth is formed at the convergence of the rays, because they did not wish to destroy so unique a specimen — even to find out the meaning of it. There seems to me little probability that the new structure is a starfish, but the old arm has been so injured that it has produced a number of new arms.

thrown off. King has found that in asterias, regeneration takes place more rapidly from the base than at a more distal level. It may appear, at first thought, that the more rapid regeneration of the arm at the place at which it is usually thrown off may be associated with its more frequent loss at this region — in other words, that the more rapid regeneration has been acquired by the region at which the arm is generally broken off. This interpretation is, however, excluded by the fact that, in general, the nearer to the base the arm is cut off, so much the more rapid is its regeneration. In other words, the more rapid regeneration of the arm at the base is only a part of a general law that holds throughout the arm. If the proposition is reversed, and it is claimed that the arm has acquired the property of breaking off at the base, because it regenerates more rapidly at that level, the following fact recorded by King is of importance, viz. that, although the arm regenerates faster at the base, yet a new arm is not any sooner produced in this way, since there is more to be produced and the new arm from the base may never catch up to one growing less rapidly from a more distal cut-surface, but having a nearer goal to reach.

The results of our examination show that those forms that are liable to have certain parts of their bodies injured are able to regenerate not only these parts, but at the same time other parts of the body that are not subject to injury. The most remarkable instance of this sort is found in those animals having breaking-joints. In these forms, we find that regeneration takes place both proximal and distal to this region. If the power of regeneration is connected with the liability of a part to injury, this fact is inexplicable.

Turning now to the question as to whether regeneration takes place in those species that are subject to injury more frequently or better than in other species, we find that the data are not very complete or satisfactory for such an examination. It is not easy to ascertain to what extent different animals are exposed to injury. If we pass in review the main groups of the animal kingdom, we can at least glean some interesting facts in this connection.

In the protozoa nucleated pieces have been found to regenerate in all forms that have been examined, including amœba, difflugia, thalassicolla, paramœcium, stentor, and a number of other ciliate infusoria.

In the sponges it has been found by Oscar Schmidt that pieces may produce new individuals, but how widely this occurs in the group is not known. In the cœlenterates many forms are known to regenerate, and it is not improbable that in one way or another the process occurs throughout the group. The hydroid forms, hydra, tubularia, parypha, eudendrium, antennularia, hydractinia, podocoryne, etc.,

the jelly-fish, gonionemus, and certain members of the family *Thau-mantidæ*, have been found to regenerate. Amongst the *Scyphozoa*, metridium, cerianthus, and the scyphistoma of aurelia regenerate, and the jelly-fishes belonging to this group have a limited amount of regenerative power.

In the platodes we find that all the triclads, thus far examined, including planaria, phagocata, dendrocœlum, and the land triclad, bipalium, regenerate. It has been shown that the marine triclads also regenerate, but less rapidly and extensively, while the marine polyclads have very limited powers of regeneration. The regeneration of the trematodes and cestodes has not, so far as I know, been studied, neither have the nematodes been examined from this point of view.

Some of the nemerteans regenerate, others do not seem to have this power. A small fresh-water form, tetrastemma, that I examined, did not regenerate, although some of the pieces, that were filled with eggs, remained alive for several months.

In the annelids we find a great many forms that regenerate — many marine polychæta have this power; all oligochæta that have been studied regenerate; both land forms, like lumbricus, allolobo-phora, etc., and fresh-water forms, like lumbriculus, nais, tubifex, etc.

In the crustacea the appendages have the power to regenerate in all the forms that have been examined.

Several kinds of myriapods, as well as a number of spiders, are known to regenerate their legs. In the insects, however, only a few forms are known to have this power, — caterpillars, mantis, and the cockroach. The large majority of insects, in the imago state, do not seem to be able to regenerate, although in a few cases regeneration has been found to occur.[1]

In the mollusks, regeneration of the head takes place under certain conditions. Spallanzani thought that if the entire head is cut off a new one regenerates. This conclusion was denied by at least eleven of his contemporaries, and confirmed by about ten others. It was found later that the result depends in part on the time of year and in part on the kind of snail. Carrière, who more recently examined the question, found that even under the most favorable conditions regen-eration does not take place if the circumœsophageal nerve-commissure is completely removed with the head, but if a part remains, a new head develops. It has been stated that a new foot regenerates in helicarion, and I have found that the foot regenerates also in the fresh-water snails, physa, limnæa, and planorbis. If the margin of the shell of a lamellibranch or of a snail is broken off, it is renewed by the mantle. The arms of some of the cephalopods are known to regenerate, particularly the hectocotylized arm.

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[1] For a review of the literature see Brindley, '98.

In all the main groups of echinoderms, with one possible exception, regeneration has been found to take place.   Probably all starfishes and brittle-stars regenerate their arms, and even if cut in two or more pieces, new starfishes develop.   The crinoids regenerate lost arms, and even parts of the disk ; also the visceral mass.   The holothurians have very remarkable powers of regeneration.   In some forms regeneration takes place if the animals are cut in two, or even in more than two pieces.   The remarkable phenomenon of evisceration that take place in certain holothurians, if they are roughly handled, or kept under unfavorable conditions, are well known and have been described by a number of writers.   It has even been suggested that the holothurian may save itself by offering up its viscera
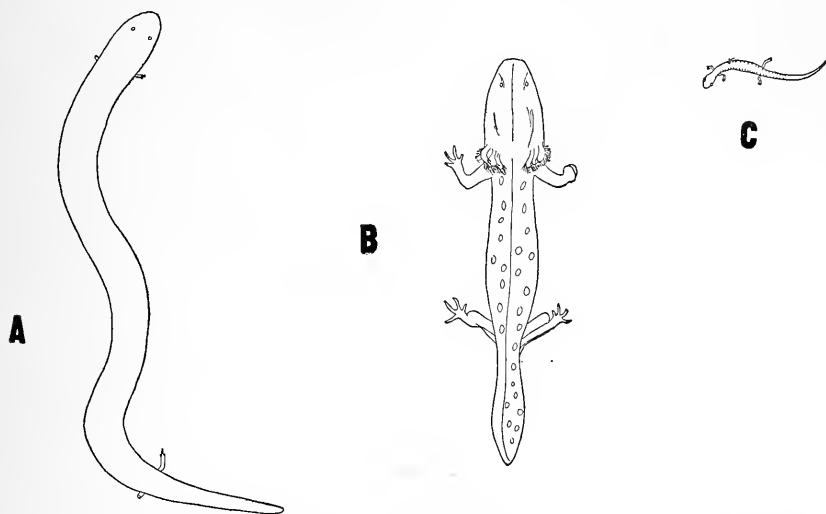


FIG. 39. — *A. Amphiuma means* with left fore and hind leg regenerating.   *B. Necturus maculatus* with right fore leg beginning to regenerate after eight months.   *C. Plethedon cinereus.   A, B, C.* Drawn to same scale.

to its assailant !   Unfortunately for this view, it has been found that the viscera are unpalatable, at least to sea-anemones and to fishes. Ludwig and Minchin suggest that the throwing off of the Cuvierian organs, which are attached to the cloaca, is a defensive act, and if carried too far, according to the latter writer, the viscera may also be lost.   The holothurians have remarkable recuperative powers and may regenerate new viscera in a very short time.   The sea-urchins form, perhaps, an exception in this group, since there are no records of their regenerative power, but no doubt this is because they have not been as fully investigated as have other forms.

In the vertebrates the lower forms, amphioxus, petromyzon, and sharks, have not been studied in regard to their regenerative power.

In the teleostean fishes the fins of a number of forms are known to regenerate. It is probable that this takes place in most members of the group.

In the amphibia we find a large number of forms that regenerate their limbs and tail, and other parts of the body, but limitations appear in certain forms. The rapid regeneration of the legs in the smaller urodeles has been often described. In larger forms it takes place more slowly, at least in large forms having large legs. In proteus the regeneration may extend over a year and a half, and in necturus it takes more than a year to make a new limb, at least in animals in confinement. In the large form, amphiuma, that has extremely small legs, regeneration takes place much more rapidly than in a form like necturus having much larger legs (Fig. 39).

In amphiuma the feet are not used by the animal as organs of locomotion, since they are too small and weak to support the heavy body. They can be moved by the animal in the same way that the feet are moved in other forms, and yet are useless for progression. It is said by Schreiber that the regeneration of the legs of *Triton marmoratus* is relatively very slight as compared with that of other forms. Fraisse also found in this form that an amputated leg did not grow again, only a deformed stump being produced. The tail also is said to regenerate to only a slight extent, but, so far as I know, there is nothing peculiar in the life of this form that makes it less liable to injury than other large urodeles.[1] Weismann cites the case of proteus, which is said also to regenerate less well than do other forms. It lives in the caves of Carniola, where there are few other animals that could attack or injure it, and to this immunity is ascribed its lack of power of regeneration; yet Goette states that he observed a regenerating leg in this form, but that the process was not complete after a year and a half. In necturus also, which is not protected in any way, regeneration is equally slow. Frogs are unable to regenerate their limbs, although they are sometimes lost, but the larval tadpole can regenerate at least its hind legs. In the lizards the tail regenerates, but at present we do not know of any connection between this condition and the liability of certain forms to injury. Turtles and snakes do not regenerate their tails. I do not know of any observations on crocodiles.

In birds, the legs and wings are not supposed to have the power to regenerate,[2] but in two forms [3] at least the beak has been found to

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[1] I do not know whether this animal was kept long enough to make it certain that the legs do not regenerate.

[2] A statement to the contrary quoted in Darwin's *Animals and Plants under Domestication* is doubted by Darwin himself.

[3] The stork and the fighting cocks.

possess remarkable powers of regeneration. There are a few very dubious observations in regard to the regeneration in man of super-fluous digits that had been cut off.[1]

These examples might be added to by others in the groups cited, and also by examples taken from the smaller groups of the animal kingdom, but those given will suffice, I think, to show that the power to regenerate is characteristic of entire groups rather than individual species. When exceptions occur, we do not find them to be forms that are obviously protected, but the lack of regeneration can rather be accounted for by some peculiarity in the structure of the animal. If this is borne in mind, as well as the fact that protected and unpro-tected parts of the same animal regenerate equally well, there is established, I think, a strong case in favor of the view that there is no necessary connection between regeneration and liability to injury. We may therefore leave this side of the question and turn our atten-tion to another consideration.

It will be granted without argument that the power of replacement of lost parts is of use to the animal that possesses it, especially if the animal is liable to injury. Cases of usefulness of this sort are gener-ally spoken of as adaptations. The most remarkable fact in connec-tion with these adaptive responses is that they take place, in some cases at least, in parts of the body where they can never, or at most very rarely, have taken place before, and the regeneration is as per-fect as when parts liable to injury regenerate. Another important fact is that in some forms the regeneration is so slow that if the competition amongst the animals was very keen those with missing legs, or eyes, or tails, would certainly succumb; yet, if protected, they do not fail to regenerate. If, therefore, the animal can exist through the long interval that must elapse before the lost part regenerates, we cannot assume that the presence of the part is of vital importance to the animal, and hence its power to regenerate could scarcely be described as the result of a "battle for existence," and without this principle "natural selection" is powerless to bring about its supposed result.

It is extremely important to observe that some cases, at least, of regeneration are not adaptive. This is shown in the case where a new head regenerates at the posterior end of the old one in *Planaria lugubris*, or where a tail develops at the anterior end of a posterior piece of an earthworm, or when an antenna develops in place of an eye in several crustacea. If we admit that these results are due to some inner laws of the organism, and have nothing to do with the rela-tion of the organism to its surroundings, may we not apply the same principle to other cases of regeneration in which the result is useful?

[1] See Darwin, *loc cit.*

So firm a hold has the Darwinian doctrine of utility over the thoughts of those who have been trained in this school, that whenever it can be shown that a structure or a function is useful to an animal, it is without further question set down as the result of the death struggle for existence. A number of writers, being satisfied that the process of regeneration is useful to the animal, have forthwith supposed that, *therefore*, it must have been acquired by natural selection. Weismann has been cited as an example, but he is by no means alone in maintaining this attitude. It would be entirely out of place to enter here into a discussion of the Darwinian theory, but it may be well worth while to consider it in connection with the problem of regeneration.

We might consider the problem in each species that we find capable of regenerating ; or, if we find this too narrow a field for our imagination, we might consider the process of regeneration to have been "acquired by selection in the lower and simpler forms," and trace its subsequent progress as it decreased in the course of phylogeny "in correspondence with the increase in complexity of organization," or with the decrease of exposure to injury. At the risk of adopting the narrower point of view I shall confine the discussion to the possibility of regeneration being acquired, or even augmented, through a process of natural selection in any particular species.

The opportunity to regenerate can only occur if a part is removed by accident or otherwise. On the Darwinian theory we must suppose that of all the individuals of each generation that are injured, *in exactly the same part of the body*, only those have survived or have left more offspring that have regenerated. In order that selection may take place, it must be supposed that amongst these individuals injured *in exactly the same region*, regeneration has been better in some forms than in others, and that this difference is, or may be, decisive in the competition of the forms with each other. The theory does not inquire into the origin of this difference between individuals, but rests on the assumption of individual differences in the power to regenerate, and assumes that these differences can be heaped up by the survival and inbreeding of the successful individuals ; *i.e.* it is assumed that, by this picking out or selection through competition in each generation of the individuals that regenerate best, the process will become more and more perfectly carried out in the descendants, until at last each part has *acquired* the power of complete regeneration.

There are so many assumptions in this argument, and so many possibilities that must be realized in order that the result shall follow, that, even if the assumptions were correct, one might still remain sceptical in regard to the possibilities ever becoming realized. If we examine somewhat more in detail the conditions necessary to bring

about this supposed process, we shall find ample grounds for doubt, and even, I think, for denial that the results could ever have been brought about in this way.

In the first place, the assumption that the regeneration of an organ can be accounted for as a result of the selection of those individual variations that are somewhat more perfect, rests on the ground that such variations occur, for the injury itself that acts as a stimulus is not supposed to have any direct influence on the result, *i.e.* for better or worse. All that natural selection pretends to do is to build up the complete power of regeneration by selecting the most successful results in the right direction. In the end this really goes back to the assumption that the tissue in itself has power to regenerate more completely in some individuals than in others. It is just this difference, if it could be shown to exist, that is the scientific problem. But, even leaving this criticism to one side, since it is very generally admitted, it will be clear that in many cases most of the less complete stages of regeneration that are assumed to occur in the phyletic series could be, in each case, of very little use to the individual. It is only the completed organ that can be used; hence the very basis of the argument falls to the ground. The building up of the complete regeneration by slowly acquired steps, that cannot be decisive in the battle for existence, is not a process that can be explained by the theory.

There is another consideration that is equally important. It is assumed that those individuals that regenerate better than those that do not, survive, or at least have more descendants; but it should not be overlooked that the individuals that are not injured (and they will belong to both of the above classes) are in even a better position than are those that have been injured and have only incompletely regenerated. The uninjured forms, even if they did not crowd out the regenerating ones, which they should do on the hypothesis, would still intercross with them, and in so doing bring back to the average the ability of the organism to regenerate. Here we touch upon a fatal objection to the theory of natural selection that Darwin himself came to recognize in the later editions of the *Origin of Species*, namely, that unless a considerable number of individuals in each generation show the same variation, the result will be lost by the swamping effects of intercrossing. If this be granted, there is left very little for selection to do except to weed out a few unsuccessful competitors, and if the same causes that gave origin to the new variation on a large scale should continue to act, it will by itself bring about the result, and it seems hardly necessary to call in another and questionable hypothesis.

Finally, a further objection may be stated that in itself is fatal to

the theory. We find the process of regeneration taking place not only at a few vulnerable points, but in a vast number of regions, and in each case regenerating only the missing part. The leg of a salamander can regenerate from every level at which it may be cut off. The leg of a crab also regenerates at a large number of different levels, and apparently this holds for all the different appendages. If this result had been acquired through the action of natural selection, what a vast process of selection must have taken place in each species! Moreover, since the regeneration may be complete at each level and in each appendage without regard to whether one region is more liable to injury than is another, we find in the actual facts themselves nothing to suggest or support such a point of view.

If, leaving the adult organism, we examine the facts in regard to regeneration of the embryo, we find again insurmountable objections to the view that the process of regeneration can have been produced by natural selection. The development of whole embryos from each of the first two or first four blastomeres can scarcely be accounted for by a process of natural selection, and this is particularly evident in those cases in which the two blastomeres can only be separated by a difficult operation and by quite artificial means. If a whole embryo can develop from an isolated blastomere, or from a part of an embryo without the process having been acquired by natural selection, why apply the latter interpretation to the completing of the adult organism?

Several writers on the subject of regeneration in connection with the process of autotomy (or the reflex throwing off of certain parts of the body) have, it seems to me, needlessly mixed up the question of the origin of this mechanism with the power of regeneration. If it should prove true that in most cases the part is thrown off at the region at which regeneration takes place to best advantage, it does not follow at all that regeneration takes place here better than elsewhere, because in this region a process of selection has most often occurred. The phenomenon of regeneration in the arm of the starfish, that has been described on a previous page, shows how futile is an argument of this sort. If, on the other hand, the autotomy is supposed to have been acquired in that part of the body where regeneration takes place to best advantage, then our problem is not concerned with the process of regeneration at all, but with the origin of autotomy. If the attempt is made to explain this result also as the outcome of the process of natural selection acting on individual variations, many of the criticisms advanced in the preceding pages against the supposed action of this theory in the case of regeneration can also readily be applied to the case of autotomy. In Chapter VIII, in which the theories of autotomy are dealt with, this problem will be more fully discussed.

# CHAPTER VI

## REGENERATION OF INTERNAL ORGANS. HYPERTROPHY. ATROPHY

It is a more or less arbitrary distinction to speak of internal in contrast to external organs, since the latter contain internal parts; but the distinction is, for our present purposes, a useful one, especially in regard to the question of regeneration and liability to injury. In this connection we shall find it particularly instructive to examine those cases of regeneration of internal organs that cannot be injured, under natural conditions, without the animal itself being destroyed. An illustration of this may be given. The liver, or the kidney, or the brain of a vertebrate can seldom be exposed to accidental injury without the entire animal being destroyed, although, of course, diseases of various kinds may injure these organs without destroying the animal, but cases of the latter kind are not common.

The experiments made by Ponfick ('90) on the regeneration of the liver in dogs and in rabbits gave the most striking results. Ponfick found after removal of a fourth, or of a half, or even, in a few successful operations, of three-fourths of the liver, that, in the course of four or five weeks, the volume of the remaining part increased, and in the most extreme case, to three times that of the piece that had been left in the body. The first changes were found to have begun as early as thirty hours after the operation, when the liver cells had begun to divide. The maximum number of dividing cells was found about the seventh day, and then decreased from the twentieth to the twenty-fifth day, but cells were found dividing even on the thirtieth day. These dividing cells appeared everywhere throughout the liver, and were no more abundant at the cut-edges than elsewhere. There takes place, in consequence, an increase in the volume of the liver, rather than a replacement of the part that is removed. The increase takes place in the cells of the old part, the lobules swelling up to two, three, or even four times their former size. No new liver lobules seem to be formed. The old tubules of the liver also become larger, owing to an increase in the number of their cells. Since the change takes place in the old part, and is due to an increase in size of the

lobules, tubes, etc., the process is spoken of as one of hypertrophy rather than of regeneration.

Kretz found a case in which the entire parenchyma of the liver seemed to have been destroyed, presumably by a poison from some micro-organism, and later a regeneration of the tissue had taken place. If this conclusion is correct, it shows that sometimes an internal organ may meet with an injury that does not directly destroy the rest of the body, and the animal may survive.

The regeneration of the salivary gland of the rabbit described by Ribbert is another example of an internal organ that can seldom be injured, and yet can be replaced after artificial removal. Weismann ('93) has recorded an experiment in which half of a lung of triton was cut off. After fourteen months the lung had not been restored in four individuals, and in one " it was doubtful whether a growth of the lung had not taken place, but even in this case it had not recovered its long, pointed form."

The regeneration of the eye in triton was first made known by Bonnet. The right eye was partly cut out, and after two months it had completely regenerated. Blumenbach, in 1784, removed the anterior part of the bulb of the eye of " *Lacerta lacustris*." Six months later a smaller bulb was present. Phillipeaux ('80) found that if the eye of an aquatic salamander was not entirely removed, a new eye regenerated ; but if the eye was completely extirpated a new eye did not appear. Colucci, in 1885, described the regeneration of the lens of the eye of triton from the edge of the optic cup. Wolff, later, independently, discovered the same fact, and it has been more recently confirmed by E. Müller ('96), W. Kochs ('97), P. Rothig ('98), and Alfred Fischel ('98). The most important part of this discovery is that the new lens develops from the margin of the optic cup, and not from the outer ectoderm, as it does in the embryo. This result will be more fully discussed in a later chapter. It is highly probable in this case that the regeneration stands in no connection whatsoever with the liability of the eye to injury, for of the large number of salamanders that have been examined, none has been found with the eye mutilated. The position of the eye is such that it is well protected from external injury, and the tough cornea covering its outer surface would also further protect it from accidental injury. When we recall the high degree of structural complexity of the eye, its capacity to regenerate, if only a portion of the bulb is left, and its power to replace the lens if this is removed are certainly very remarkable facts. We find here, I think, an excellent refutation of the incorrectness of the general assumption of a connection between regeneration and liability to injury. Moreover, since there is no evidence whatsoever to show that the eyes in these animals are ever

subject to diseases caused by bacteria, and much evidence to show that they are not so injured, we are still further confirmed in our general conclusion.

It has been known for a long time that even in man the lens of the eye is sometimes regenerated after its removal. The regeneration has been supposed to take place from the old capsule of the lens, or possibly from a piece of the lens left after the operation; but whatever its origin, the fact of its regeneration in man, and in other mammals also, is a point of some interest in this connection.

Podwyssozki ('86) found that regeneration may take place in the kidney of certain mammals, — best in the rat, more slowly in the rabbit. The restoration of the lost part takes place first by replacement of the epithelium. The old canals may then push out into the connective tissue that accumulates in the new part, but there is no new formation of canals or of glomeruli. According to Podwyssozki the regeneration of the kidney is less complete than that of any other gland. Peipers has reinvestigated the subject, and his results agree in the main with those just given. He finds in addition that new canals may grow out from the old ones into the new part.

Podwyssozki and Ribbert ('97) have found that the salivary gland has a remarkable power of regeneration. Ribbert removed a half (or even more than this) of the salivary gland of the rabbit. In the course of two or three weeks new material had developed over the cut-surface. In one case at least five-sixths of the gland had been taken out, and at the end of three weeks the gland had regenerated to its full size. Microscopic examination showed that the greater part of the gland was made up of new lobes, some of which were as large as, others smaller than, the normal lobes. The new part contained new tubes with terminal acini. These had arisen from the tubes of the old part. The connective tissue of the new part also came from that of the old. In this case a true process of regeneration takes place from the cut-surface; in addition a certain amount of enlargement, or hypertrophy, also takes place in the old part. Ribbert believes there is a connection between the process of hypertrophy and of regeneration of such a kind that the more active the one, the less active the other.

Regenerative changes are known to occur in other internal organs besides these glandular ones. Broken bones are united, if brought in contact, by a process that involves a certain amount of regeneration. Although new bony tissue may be formed at the region of union, the bones of mammals and of birds do not seem able to complete themselves, if a part is removed, except to a limited extent. While the broken bones of the leg or of the arm have the power of reuniting if held for some time in place, yet in nature this condition can seldom

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be fulfilled, and the animal with a broken leg or wing will most probably be killed. Nevertheless, since the bones have this power at whatever level they may be broken (but only if they are kept together artificially), the process can scarcely have been acquired through the liability of the parts to injury. We find here another instance of a useful process existing in animals, but one that could not have been acquired by exposure of the part to injury. It is probable that this same property is found in all the bones of the body,—in those that may occasionally be injured, and in those that are not.

The muscles have also the power of regenerating, although few experiments have been made except in those forms in which the whole leg can regenerate, yet there are a few observations that show that even in mammals, in which the leg or the arm cannot regenerate as a whole, a certain amount of regeneration of the muscles themselves may take place.

It has been known for a long time that if a nerve is cut a new nerve grows out from the cut-end, and may extend to the organs supplied by that nerve. The process takes place more successfully if the peripheral part is left near the cut-end from which the new nerve grows. Whether this old part only serves to guide the new part to its proper destination, or whether it may also contribute something to the new nerve, as, for instance, cells for the new sheath, is not finally settled. The general opinion in regard to the origin of the new nerve fibres is that the central axis or fibril grows from the cut-end. That this power could have been acquired for each nerve as a result of its liability to injury is too improbable to discuss seriously.

The central nervous system of the higher vertebrates seems to have very little power of regeneration, and although in some cases a wounded surface may be covered over and a small amount of connective tissue be formed, the development of new ganglion cells does not seem to occur. In other animals, as the earthworm, planarian, and even in the ascidian, as shown by Loeb, a new entire brain may develop after the removal of the old brain, or of that part of the body in which it is contained.

This examination of the power of regeneration of internal organs in the vertebrates has shown that it is highly improbable that there can be any connection between their power of regeneration and their liability to injury. That the internal organs may be occasionally injured by bacteria, or by poisons made in the body, may be admitted, but that injuries from this source have been of sufficient frequency to establish a connection, if such were indeed possible, between their power of regeneration and their liability to injury from these causes is too improbable a view to give rise to much doubt. These results taken in connection with those discussed in the preceding chapter go

far toward disproving the view that the power of regeneration has a connection with the liability of a part to injury.

## HYPERTROPHY

The hypertrophy, or unusual enlargement, of organs has long attracted the attention of physiologists, and the extremely interesting observations and experiments that have been made in this connection have an important although an indirect bearing on the problem of regeneration. Ribbert, as has been pointed out, holds that the processes of hypertrophy and of regeneration stand in a sort of inverse relation to each other, but it is doubtful, I think, if any such general relation exists. Two kinds of hypertrophy are now generally distinguished : functional hypertrophy, which takes place when a part becomes enlarged through use ; and compensating hypertrophy, which takes place when one organ being removed another enlarges. The enlargement in the latter case may, of course, be brought about by the increased use of the parts that enlarge, but as this is not necessarily the case, the distinction between the two processes is a useful one. The causes of compensating hypertrophy are by no means simple, and several possibilities have been suggested to account for the enlargement. The best ascertained facts in connection with hypertrophy relate almost entirely to man and to a few other mammals.[1]

By hypertrophy is meant an increase of the substance of which an organ is composed. Swelling due to the imbibition of water or of blood-serum is not, in a technical sense, a process of hypertrophy. Virchow distinguishes two kinds of hypertrophy : (1) Hypertrophy in a narrower sense in which the enlargement is due to an increase in the size of the cells of which an organ is composed. This enlargement of the individual cells leads of course to an increase in the size of the whole organ. (2) Hyperplasy due to an increase in the number of cells of which an organ is composed, which also causes an enlargement of the whole organ if the cells retain the normal size. ' The division into functional and compensating hypertrophy given above is a physiological distinction, and both of these processes might occur in Virchow's subdivisions.

Giants may be looked upon as hypertrophied individuals, since all the organs of the body are larger than the normal. The enlargement is, in this case, not due to external influences, but to some peculiarity

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[1] The more generally accepted results are given in Virchow's *Cellular Pathology* and in Ziegler's *Pathological Anatomy*. An excellent review of the subject down to 1895 is given in a summary by Ludwig Aschoff in the *Ergebnisse d. allgem. patholog. Morphol. und Physiologie*, 1895, " Regeneration und Hypertrophie," in which there are two hundred and eighteen references to the literature.

of the organism itself. Whether the size is due to more cells being present, as seems probable, or to the cells being larger, or to both, has not, so far as I know, been determined for man. In a mollusk, *Crepidula fornicata*, in which large and small adult individuals occur, it has been shown by Conklin ('98) that the difference is due entirely to the larger number of cells in the larger individual. In this case external conditions, in so far as they retard the maximum possible growth of the individual, are responsible for the differences in size. The distinction is, in this case, rather between large normal individuals and dwarfs, than between giants and normal or average individuals.

The voluntary muscles of the body of man grow larger, and may be said to hypertrophy, as a result of doing certain kinds of work. The muscles of the hand and arm grow large through use, and become smaller again if not used ; but the muscles of the fingers of a musician do not hypertrophy, although the total amount of work done may be very large. It is only when muscular work is done against great resistance that enlargement of the muscles takes place. The factors that may bring about the enlargement will be discussed later.

The kidneys seem to give the most satisfactory evidence of compensating hypertrophy. Nothnagel[1] states that it has been shown in man, in the rabbit, and in the dog, that when one kidney has been removed the other enlarges ; and that this takes place both for young animals, in which the kidneys have not reached their full size, and in adult animals, in which the remaining kidney becomes larger than normal. In the adult the enlargement is due to hypertrophy, in Virchow's sense, in the tubules and in the epithelium of the canals. In the young animal there is, in addition, a hyperplastic growth that leads to an increase in the number of glomeruli, etc.

Experiments have shown that the same amount of urea is excreted by the animal after the removal of one kidney as before ; in fact, this is true immediately after the operation, before any increase in the size of the organ has taken place. This means that, under normal conditions, the kidneys do not perform their maximum of work. It is important to observe in this connection that the remaining kidney gets more blood than it would get if the other were present. Nothnagel sums up the changes that take place in this way : First, the removal of one kidney ; second, an increase in the flow of blood in the remaining kidney ; third, an increase in the functional activity and excretion of this kidney ; fourth, along with the increase in the flow of blood, there is a necessary increase in the amount of food that is

[1] Nothnagel gives a review of the subject down to 1886 in an article entitled "*Über Anpassung und Ausgleichung bei pathologischen Zuständen. Zeitsch. f. klinische Medicin.*" 1886. Vols. X and XI.

brought to the kidney in the blood; fifth, this food is taken up in larger amount than before by the cells, which leads to an increase in the growth of the cells, which produces hypertrophy. The increase in size, looked at from this point of view, Nothnagel says, has nothing mysterious about it. The enlargement seems to be an adaptation; but the enlargement does not take place because it is an adaptive process, but because it cannot be helped under the conditions that arise. We shall return again to Nothnagel's interpretation, when we come to consider other views.

Experiments of the sort just described are most easily carried out on the paired organs of the body, such as the salivary glands, the tear glands, the mammæ of the female, and the testes of the male. In regard to the latter two organs the evidence, especially in the case of the testes, is conflicting, but the recent experiments of Ribbert seem to give definite results. Nothnagel had found that after the removal of one testis there is no hypertrophy of the other. He pointed out that this result does not stand in contradiction to his hypothesis in regard to the kidneys, for the loss of one testis does not lead to a greater functional activity in the other. Each acts for itself alone. The result shows further, he adds, that the process of hypertrophy is not an adaptive one, but a physical or a physiological process. Ribbert on the contrary thinks that even Nothnagel's statistics give evidence of hypertrophy, and Ribbert's own experiments give unmistakable evidence of a considerable enlargement of the remaining testis. In his experiments, young rabbits were used that were born of the same mother and in the same litter. One of the testes was removed from some of the individuals, and after some months the remaining testis was taken out and its weight compared with that of the control animal. In sixteen out of seventeen experiments there was found to be a noticeable increase in the single testis as compared with either testis of the control animal. The results show that in some cases the single testis weighs almost as much as the two together of the control animal. It is important also to notice that in this case the enlargement has taken place in an organ that has not been active, as was the case with the kidney.

Ribbert has also shown that hypertrophy takes place in the mammæ of the rabbit after the removal of some of them. Five out of the eight mammæ were removed in three cases, and seven out of the eight in two other cases from young rabbits about two months old. Ribbert found that if the operator is not careful to remove completely all the tissue of a mamma an active regenerative process takes place from the part that remains. After five and a half months the single remaining mamma of one animal measured six and one-half by three and four-fifths centimetres, and the corresponding one in the control

animal five and three-fourths by three and one-half centimetres. The glandular tissue was also found less developed in the control animal.

In another experiment the rabbit experimented upon bore young when it was six and a half months old. Soon after the birth of the young and before the mamma had been used the animal was killed and the single mamma that had been left was measured. It was much enlarged and projected more than the normal mammæ. It measured nine by five centimetres. In a normal control animal[1] the corresponding mamma measured seven by five centimetres. The number of acini was in the proportion of sixteen in the animal operated upon to ten in the normal. The results show a distinct compensating hypertrophy, due to a hyperplastic increase in the number of elements of the gland.

A further example of compensating hypertrophy has been found after the removal of the spleen, when the lymphatic glands of other parts of the body become enlarged. There are also observations which go to show that after the removal of some of the lymphatic glands others undergo an enlargement.

Ziegler[2] has given a critical review of the various opinions and hypotheses that have been advanced to account for the process of hypertrophy. According to Cohnheim[3] hypertrophy in bones, muscles, spleen, and glands is due to hyperæmia, *i.e.* increased blood supply. He thinks that neither mechanical nor chemical stimuli can cause directly new processes of growth. Recklinghausen[4] thinks that hypertrophy is not due to any extent to an increase in the food supply. Samuel[5] explains hypertrophy as due to a removal of, or to a decrease in, the resistance to growth and also to the influence of the nerves. Klebs[6] thinks that three factors enter into the problem, (*a*) inherited peculiarities, (*b*) overfeeding, (*c*) a removal of the controlling influences. Weigert believes that reparative processes are due to the removal of influences that prevent growth, and not to a direct stimulus. He thinks that a stimulus may start a functional act, but can never start a nutritive or a formative one. Good nourishment, for instance, may bring a tissue to a maximum development that is predetermined by innate peculiarities, but "idioplastic forces" are not thereby increased. Pekelharing[7] thinks that hypertrophy is due to a disappearance of a resistance to growth, and also to a stimulus causing proliferation.

We see from these various opinions how little is really known;

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[1] Not, however, from the same litter.

[2] *Internat. Beiträge zu wissensch. Medicin. Festschrift für R. Virchow*, Vol. II, 1891.

[3] *Vorlesungen über allegemeine Pathologie*, Vol. I, 1882.       [4] *Handbuch.*

[5] *Handbuch d. allgem. Pathologie*, 1879.       [6] *Allgemeine Pathologie*, Vol. II, 1889.

[7] *Über Endothelwucherungen in Arterien. Beitr. z. pathol. Anat.*, Vol. VIII, 1890.

how little has been determined as yet by experiment as to the causes that bring about hypertrophy. Many of the views are more or less plausible in the absence of direct, experimental evidence, but it remains for the future to decide as to the correctness of all of them. They are valuable as suggestions, in so far as they show the different possibilities that must be taken into account.

Ziegler first advocated the view, in the first edition of his *Lehrbuch*, that hypertrophy is due to a lessening of the resistance to growth. He thinks that while hyperæmia and transudation may support the new growth, they are never the only cause of the formation of new tissue. While Virchow's view that any injury to the body or to an organ excites proliferation finds support in the work of Stricker and Grawitz, yet the view has been combated by Cohnheim and by Weigert, and is no longer held by many pathologists. Ziegler points out that as a result of his own work, and that of his students, traumatic and chemical lesions are not followed at once by new growth of the tissue, but by degeneration of the tissue, and by changes in the circulation that lead to exudations. The new growth begins, at the earliest, eight hours after the operation, and generally only after twenty-four hours. Also after mechanical, chemical, or thermal injuries, a long interval elapses before phenomena of growth begin. The injury itself does not appear to produce the growth, but brings about those conditions that lead to cell-multiplication. Ziegler discusses what is meant by the idea of a lessening of the resistance to growth. He himself does not mean by this that hypertrophy depends on changes in the physical conditions, because it is known that living phenomena are the outcome of chemical processes and it is, therefore, *à priori* probable that the effect is brought about by chemical substances in the fluids of the tissues. These substances affect functional actions, and may even bring about regenerative changes. This action of chemical substances on the formative activity of the cell is theoretically possible in either of two ways; first, chemical substances of definite concentration are set free, or, second, chemical substances are present in the normal condition that prevent proliferation, but if their influence should be counteracted by other substances the conditions become favorable to growth. It is known in the case of certain unicellular organisms, that derive their nourishment from the surrounding medium, that their increase in number may be retarded by the presence of certain chemical substances. It is also known that certain organisms may themselves produce chemical substances that prevent their own multiplication. It is, therefore, at least conceivable that after a part has been injured a new substance may be produced that acts upon and destroys in the organ itself the substances there present that have prevented its further growth. The other interpretation is that

in the breaking down of the tissue of the organ a substance is produced that excites the cells to proliferation.

Klebs suggested that the accumulation of the leucocytes at the wounded surface may act as a stimulus to growth, and that the chromatin of their nuclei might be absorbed by the cells of the tissue, and combining with the nuclei of these cells bring about the new growth. But Ziegler points out that we now know that although the leucocytes are dissolved and absorbed over the wounded surface, no process of absorption, of the sort postulated by Klebs, takes place. Ziegler thinks that Nothnagel is wrong in supposing that an increase in the blood supply, bringing with it an increase in the nourishment, can account for the hypertrophy of the kidney. On the contrary he believes that the growth is the result of an increase in the function of the organ due to the increase of the chemical substance, urea, that is brought to the secreting cells. The muscles of the body also hypertrophy as a result of their activity and not as a result of the additional blood supply.

In connection with these problems of hypertrophy it may be pointed out that, under certain conditions, blood vessels may enlarge and their walls become thickened. To cite a single example, Nothnagel found that if the femoral artery of the rabbit is tied, the blood vessels, that come off immediately above the ligature, and which have already, through their subdivisions, connections in the muscles with other branches of the same femoral artery (that come off below the ligature), grow larger after a time. This he believes to be due, in the first instance, to the increased speed of the blood in the vessels, and thereby the bringing to these arteries of an increased food supply. Other writers have given different interpretations. Ziegler himself believes that several factors may be capable of bringing about the result. He thinks it improbable that the increase in the food supply can alone be the cause, and thinks it much more probable that the increased work that the vessels must perform while carrying more blood will account for the enlargement.

In connection with this discussion it may not be unprofitable to recall that in the regeneration of the lower animals we find simpler conditions in which proliferation of the cells takes place under circumstances where many of the factors suggested in the above discussion are absent. In the first place we find that new growth may occur without any increase in the nourishment that is brought to the organ. Regeneration takes place in the entire absence of food, except so far as it may be stored up in the tissues. Even in a planarian that is starving and decreasing in size, proliferation of new cells will take place if a part is removed. In many of the lower forms there may be proportionately even a much greater proliferation than in the regeneration and hypertrophy in the mammalian organs. It is true

that proliferation may be more active if the tissues are well fed, but this does not show that the presence of food is a factor in the proliferation except so far as it keeps the proliferating cells in their best condition for growth. It is possible in many animals, more especially in some of the lower forms, to force them to grow rapidly by supplying them with a large amount of food, and conversely by decreasing the food to delay the growth. While this shows that the rate of growth is, within certain limits, a function of the amount of food, there may be also other factors that enter into the result, and in all cases there is an upper limit beyond which it is not possible to make the animal grow any larger.

That the presence of certain substances may bring about the enlargement of a part must be admitted as probable. It has been shown, for instance, that after the removal of certain lymphatic glands other glands may become larger. This appears to be due to the greater activity of the gland, brought about probably by the presence of an increased amount of some specific substance. In this instance the result can scarcely be due to a decrease in the physical resistance to growth or to an increase in the blood flow, except so far as this is brought about by the increased activity. It is, of course, possible, even if it cannot be positively shown in the case of the lymphatic glands, that a substance in the blood causes the hypertrophy in certain organs, while in others, as in the kidney, an increase in the blood flow may be also a factor in its hypertrophy.

The view held by several pathologists, that hypertrophy and regeneration may be caused by the removal of a physical resistance to growth, cannot be looked upon as a very probable hypothesis. The experiments in grafting of hydra and lumbriculus show that regeneration may still take place when the physical resistance has been reëstablished by grafting two pieces together. These results, which are more fully described in a later chapter, demonstrate that the growth is due to other influences.

A comparison with the lower animals shows that proliferation takes place when all but three of the factors considered in connection with hypertrophy and regeneration in the higher forms have been eliminated. These are, first, the action of substances that act either directly or as counteracting some substance already present, as Ziegler suggests ; second, an innate tendency in the organism to complete itself; and, third, the use of the organ. It is impossible that the second factor enters into the problem of hypertrophy. In those cases in which regeneration takes place when a part of an organ is removed, as in the case of the liver, for example, the result may possibly also involve the second of the two factors, for the process is much like that of morphallaxis in the lower animals.

If it be granted that the growth in a hypertrophied organ is brought about by some substance that increases the function of that organ, can we suppose the phenomenon of regeneration to be due to similar factors? In other words, can we reduce both phenomena to the same principle? The case is complicated by two facts that may be illustrated by concrete examples. If a piece is cut from the middle of the body of lumbriculus new cells are produced at both ends of the piece. If we suppose the proliferation is brought about by the accumulation of certain substances in the piece, we must still invoke other factors to account for the differentiation of the proliferated material, since a head forms at one end and a tail at the other. All the hypothesis can do in itself is to account for a proliferation, not for the differentiation, and, both in the case of hypertrophy and in that of regeneration, it is the formation of new structures that we are chiefly concerned with, rather than the simple act of growth or of proliferation. If a piece of a hydra is cut off, the whole piece changes into the typical hydra form. Here there is no extensive process of proliferation, and the change is in the old part. It seems highly improbable that the production of substances in the piece could account for its change of form. These examples will suffice to show that in the process of regeneration it is very improbable that the change is brought about by special substances that may develop or be present in the part. We must suppose that during regeneration the formation of the typical form is not the result of a stimulus originating in a chemical substance acting upon the living material, but due to changes brought about directly in the living part itself. We must conclude, therefore, that despite the apparently close connection between the phenomena of hypertrophy of uninjured organs and of regeneration, they may often involve different factors.

If specific substances can bring about the hypertrophy of an organ, it is still not clear at present whether they do so by directly causing new growth, or whether their presence only stimulates the organ to greater activity and the activity of the organ is the cause of its growth. Since it must be supposed that in each organ a different specific substance brings about its activity and the consequent hypertrophy, it seems more probable that the result is due to the activity itself rather than to a stimulus from the substance. This view is further supported by the fact that in the case of the muscles and of the blood vessels the hypertrophy is directly connected with their use. The greater use brings about a larger supply of blood, but the blood is only different in amount and not in its quality. It must be confessed that it is difficult to see how the use of a part could make its growth increase, for by use the tissues break down; and we are not familiar with any other processes within the body that make for the

building up of an organ in more than an inverse ratio to its breaking down. We are, however, familiar with phenomena of building up due to an increase in the food supply. It might appear from this to be more in accordance with what we find, to assume that the hypertrophy is solely due to an increase in the food supply; yet there are other facts known that show that an organ does not increase in size simply because it gets more blood, and that this occurs only when the organs have a greater functional activity. It is a safer conclusiou, I think, at present to assume that both the activity of the organ and the increase in its supply of food acting together are factors in the result. On the other hand we are so much in the dark concerning the functioning and growth of organs that we can do little more, as the preceding pages show only too clearly, than speculate in the vaguest sort of way as to what changes take place; but since the processes seem to be within reach of experimental methods we can hope in the near future to learn more of how the processes of hypertrophy are brought about.

### *ATROPHY*

It would not be profitable to enter into a general discussion of the many cases of absorption, or of atrophy of parts of the organism, but a few examples may be given that have a general bearing on the topics discussed in this chapter. The more noticeable cases arise through disuse of an organ, as shown, for example, in the decrease in size of the muscles of man when they are not used. Since this may take place in a single group of disused muscles, when no such change occurs in other muscles of the same individual that are in use, the most obvious explanation is that the decrease is due directly to disuse. Since the blood that goes to all the parts is the same, the diminution cannot be ascribed to any special substance in the blood. The flow of blood into the disused muscle is less than when the muscle is used, and it might be supposed that atrophy is directly caused by the lessened nourishment that the muscle receives. There is also the possibility that the decrease is brought about by the accumulation of certain substances in the disused muscle itself, but since, in general, the breaking down of the muscle is most active when it is used, it seems improbable that the result can be due directly to this cause, unless indeed it could be shown that the substances produced by a disused muscle are different from those in an active muscle.

Lack of food, as is known, may cause organs to decrease, the fat first disappearing, and then in succession in vertebrates, the blood, the muscles, the glands, the bones, and the brain. Certain poisons

may also affect definite organs and bring about a decrease in size, as when the thymus and mammæ decrease from iodine poisoning, and certain extensor muscles after lead poisoning. Atrophy may also be brought about by pressure on a part, as when the feet or waist are compressed. In old age there may be a decrease in some of the organs, as in the bones, the testes and ovary, and even in the heart.

Degenerative changes appear even in the young stages of some animals, as when the tail of the tadpole is absorbed and the arms of the pluteus of the sea-urchin are absorbed by the rest of the embryo.

Especially interesting are the cases of absorption that take place when organs are transplanted to unusual situations in the body. Zahn transplanted a fœtal femur to the kidney, where it continued to grow but was later absorbed. Fischer transplanted the leg of a bird's embryo to the comb of a cock, where it continued at first to grow, but after some months degenerated. The spleen, the kidney, and the testis have been transplanted, but they degenerate, and, in general, the larger the transplanted piece the more probable its degeneration. Small pieces of the skin have been transplanted from one individual to another, and it has been found that small pieces maintain themselves better than large pieces. Ribbert's recent experiments in transplanting small pieces of different organs have been more successful than earlier experiments in which larger pieces were used. The first difficulty seems to be in establishing a blood supply to the new part, in order to nourish it. If the piece is quite small, it can absorb the substances, necessary to keep it alive, from the surrounding tissues, until the new blood supply has developed.

In the lower animals grafting experiments have been more successful, because the parts can remain alive for a longer time. It is important to find, however, that even in these cases, a part grafted upon an abnormal region of the body is usually absorbed. Rand shows that if the tentacles of hydra become displaced, as sometimes happens when a piece containing the old tentacles regenerates (Fig. 48, $A$–$A^3$), the misplaced tentacles are absorbed; and I can confirm this result. In hydra, the hollow tentacles are in direct communication with the central digestive tract, and a displaced tentacle seems to be in as good a position as a normal one, as far as its nourishment is concerned, yet it becomes absorbed.

Rand also found, in other experiments, that when the anterior end of a hydra is grafted upon the wall of another hydra, the piece may maintain itself if it is large; but it is slowly shifted toward the base of the hydra to which it is grafted, and then the two separate in this region. If the graft is small, it may be entirely absorbed into the wall of the animal to which it is attached.

Marshall found that if the head of a hydra is partially split in two,

each half-head completes itself (as Trembley had already shown). The body then begins slowly to separate into two parts, beginning at the angle between the two heads, until finally the two parts completely separate. King (1900) has repeated the experiment in a large number of cases with the same result. It seemed that the division might be brought about by the weight of the halves causing the gradual separation of the body, but King has shown that this is not the case, for, when a double form remained hanging with its head down, it still divided into two parts (Fig. 47, *A*). In this case, the weight of the two heads would cause the parts to come together rather than to separate, if gravity had any influence of the sort suggested. Marshall and King have also shown that if the posterior end of a hydra is split in two, the two parts do not continue to separate, but one of the two, if the pieces have been split some distance forward, may become constricted from the other, and, producing new tentacles at its apical end, become a new individual.

I have carried out a series of experiments on planarians of a somewhat similar nature. If the posterior end is split in two, the separation extending into the anterior part of the worm (Fig. 44, *C*), each half completes itself, but the halves do not separate unless they happen to tear themselves apart. If one of the pieces is cut off, not too near the region of union with the other half, a new posterior end, replacing that cut off, regenerates. If, however, the piece is cut off quite near the region or union of the halves, the piece that is left may be absorbed.

The absorption of misplaced parts in the lower animals cannot be explained, I think, by any lack of nutrition, especially in the case of the tentacles of hydra. The result may be due either to the displaced part not receiving exactly those substances, perhaps food substances, that it gets in its normal position, or it may be due to some formative influence. At present we are not in a position to decide between these alternatives, and, while the former view seems more tangible, and the latter quite obscure, the latter may nevertheless be found to contain the true explanation. If the view that I have adopted in regard to the organization — namely, that it can be thought of as acting through a system of tensions peculiar to each kind of protoplasm — is correct, it may be possible to account for the absorption of misplaced parts by some such principle as this.

### INCOMPLETE REGENERATION

A somewhat unusual process of regeneration takes place when the jelly-fish, *Gonionemus vertens*, is cut into pieces. As first shown by Hargitt, the cut-edges come together and fuse, and the pieces

assume the form of a bell, but the missing parts are not replaced.[1]  **I**
have worked on the same form and obtained substantially the same
results.   If the jelly-fish is cut in two, as indicated by the dotted line
in Fig. $39\frac{1}{2}$, $A$ and $A'$, each half closes in and assumes the form
shown in $B$, $B$.   Each new jelly-fish has only the two original radial
canals that each half had when separated from the other.   A faint
line along the region of fusion of the pieces seems to represent a
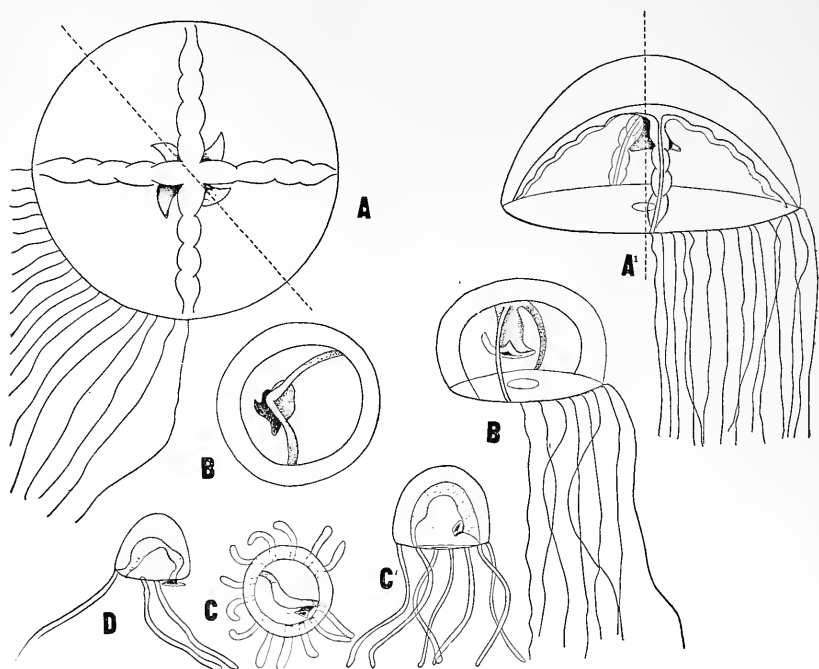new radial canal, — it is not represented in the figures, — and each



FIG. $39\frac{1}{2}$. — $A$. Aboral view of *Gonionemus vertens*.   $A^1$. Side view of same.   Dotted line in each
indicates where jelly-fish was cut into halves.   $B$, $B$. New individual from a half.   As seen
from above and from the side.   $C$, $C^1$. New individuals from a $\frac{1}{4}$ piece.   As seen from above
and from the side.   $D$. New individual from a piece less than $\frac{1}{4}$.   It contained a part of one
of the radial canals.   A new proboscis with mouth regenerated in all pieces, but no new
canals or tentacles.

half-proboscis has completed itself.   There are not formed any new
tentacles, except perhaps one, or a few more, where the cut-edges
meet.   Thus there is actually very little regeneration, although the
typical jelly-fish form is assumed by the half-piece.   If a jelly-fish
is cut into four pieces, each piece containing one of the radial
canals, the pieces also assume the bell-like form, as shown in
$C$, $C'$.   A new proboscis develops from the proximal end of the
old radial canal, and since this end is often carried to one side

[1] Haeckel (1870) first showed, in another medusa, that pieces produce new medusæ.

during the closing in of the piece, the new proboscis lies not at the top of the sub-umbrella space, but, as seen in the figure, quite to one side. Pieces even smaller than these one-fourth jelly-fish will assume the bell-like form, especially if they contain a bit of the margin of the old bell and a part of one of the radial canals, as shown in Fig. $39\frac{1}{2}$, $D$. Although I have kept these partial medusæ for several weeks, and have fed them during this time, I have found that the missing organs do not come back. That these pieces do undergo a certain amount of regeneration is shown by the formation of a new proboscis, and, in certain cases, a new radial canal. Even the tentacles may be partially regenerated, as Hargitt has shown, — especially, as I have found, if the margin of the bell is cut off very near the base of the line of tentacles. Small knobs appear along the cut-edge, but the pieces die before regeneration goes very far. If, however, the margin is cut off in only one quadrant, new tentacles may be produced along the cut-edge.

# CHAPTER VII

## PHYSIOLOGICAL REGENERATION. REGENERATION AND GROWTH. DOUBLE STRUCTURES

DURING the normal life of an individual many of the tissues of the body are being continuously renewed, or replaced at definite periods. The replacement of a part may go on by a process of continuous growth, such as takes place in the skin and nails of man, or the replacement may be abrupt, as when the feathers of a bird are moulted. It is the latter kind of process that is generally spoken of as physiological regeneration. In the same animal, however, certain organs may be continually worn away, and as slowly replaced, and other organs replaced only at regular intervals.

Bizozzero has made the following classification of the tissues of man, on the basis of their power of physiological regeneration. (1) Tissues made up of cells that multiply throughout life, as the parenchyma cells of those glands that form secretions of a definite morphological nature; the tissues of the testes, marrow; lymph glands, ovaries; the epithelium of certain tubular glands of the digestive tract and of the uterus; and the wax glands. (2) Tissues that increase in the number of their cells till birth, and only for a short time afterward, as the parenchyma of glands with fluid secretions, the tissues of the liver, kidney, pancreas, thyroid, connective tissue, and cartilage. (3) Tissues in which multiplication of cells takes place only at an early embryonic stage, as striated muscles and nerve tissues. In these there is no physiological regeneration.

There are many familiar cases of periodic loss of parts of the body. The hair of some mammals is shed in winter and in summer. Birds renew their feathers, as a rule, once a year. Snakes shed their skin from time to time. The antlers of deer are thrown off each year, and new ones formed accompanied by an increase in size and branching of the antlers. In other cases similar changes may be associated with certain stages in the life of the animal. The milk-teeth of the mammals are lost at definite periods, and new teeth acquired.[1] The larval exoskeleton of insects is thrown off at intervals, and after

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[1] In rodents, however, the incisors continue to grow throughout the life of the animal.

each moult the body increases in size; but after the pupa stage is passed and the imago formed, there is no further moulting. In the crustacea, on the other hand, the adult animals moult from time to time, and the upper limit of size is less well defined than in the insects. The larvæ also pass through a series of moults.

An interesting case of physiological regeneration has been described by Balbiani in a unicellular form, stentor. From time to time a new peristome appears along the side, moves forward and replaces the old peristome, that is absorbed as the new one comes into position. In other infusoria the peristome may be absorbed before encystment, and a new one appear when the animal emerges from the cyst. Schuberg states that when division takes place in bursaria the new peristome develops on the aboral piece in the same way as after encystment; and Gruber observed that, when an aboral piece of an infusorian is cut off, a new peristome develops in the same way as after normal division of the animal. These observations indicate that the process of physiological regeneration may follow the same course and probably involves the same factors as the process of restorative regeneration.

Tubularia absorbs its old hydranth-heads if placed in an aquarium, and regenerates new ones. It may even absorb the hydranth while growing in an aquarium, as Dalyell has shown, and presumably, therefore, also under natural conditions. After each regeneration the new stalk behind the head increases in length.

In plants, in which there is a continuous apical growth, new parts are being always added at the end of the stem, and old parts are continually dying, as seen in palms. Most trees and shrubs in temperate climates lose their leaves once a year and produce new ones in the spring. Since the new leaves develop from the new shoots at the end of the stem and branches, the old ones can, only in a general way, be said to be renewed.

That a very close relation exists between the process of physiological regeneration and restorative regeneration will be sufficiently evident from the preceding illustrations. We do not gain any insight into either of the processes, so far as I can see, by deriving the one from the other, for the process of restorative regeneration may be, in point of time, as old as that of physiological regeneration. This does not mean, of course, that the same factors may not be present in both cases. So similar are the two processes that several naturalists have attempted to show how the process of restorative regeneration has been derived from physiological regeneration. Barfurth, recognizing the resemblance between the two processes, speaks of restorative regeneration as a modification of physiological regeneration, and Weismann also supports this point of view. He says: " Physiological

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and pathological regeneration obviously depend on the same causes, and often pass one into the other, so that no real line of demarcation can be drawn between them. We nevertheless find that in those animals in which the power of regeneration is extremely great physiologically, it is very slight pathologically. This proves that a slight power of pathological regeneration cannot possibly depend on a general regenerative force present within the organism, but rather that this power can be provided in those parts of the body which require a continual, periodic regeneration; in other words, the regenerative power of a part depends on adaptation." It is, I think, erroneous to state "that in those animals in which the power of regeneration is extremely great physiologically, it is very slight pathologically." All that we are justified in concluding from the evidence is that in some cases in which physiological regeneration takes place, as in the vertebrates, pathological (restorative) regeneration may not be well developed; but even in these forms restorative regeneration is certainly present, and present especially in internal organs, as in the salivary gland, in the liver, and in the eye, which are little exposed to injury. How far physiological regeneration takes place in the tissues of the lower animals we do not know at present, except in a few cases, but far from supposing it to be absent, it may be as well developed as in higher forms. Weismann's further conclusion, that because in some animals physiological regeneration is very great and restorative regeneration very slight, therefore the latter cannot "depend on a general regenerative force within the organism," is, I think, quite beside the mark. In this connection we should not fail to notice a difference between these two regenerative processes that several writers have also called attention to, viz. that the power of cell-multiplication and the formation of new cells in each kind of tissue does not carry with it the power of restorative or even of physiological regeneration, in cases where several kinds of tissue make up an organ. For instance, if the leg of the mammal is cut off, the old cells may give rise to new ones, but the processes that would bring about the formation of the new leg are not present, or, rather, if present, cannot act. Thus, although the production of new cells from each of the different parts of the leg of a mammal may take place, yet the conditions are unfavorable to the subsequent formation of a new leg out of the proliferated cells. We should not infer that this power does not exist, but that under the conditions it cannot be carried out. The assumption that physiological regeneration is the forerunner of restorative regeneration, in the sense that historically the former preceded the latter and furnished the basis for the development of the latter, cannot be shown, I think to be even probable. This way of looking at the two processes puts them, I believe, in a

wrong relation to each other. We find both processes taking place in the simplest forms as in the unicellular protozoa, and present throughout the entire animal kingdom without any connection, excepting so far as they both depend on the general processes of growth characteristic of each organ and of each animal. This leads us to consider the general question of regeneration in its relation to the phenomena of growth.

## REGENERATION AND GROWTH

It has been pointed out in several cases in which external factors influence the growth of a plant, or of an animal, that the same factors play a similar part in the regeneration. The action of gravity on the growth of plants has been long known, and that it is a factor in the regeneration of a piece of a plant has also been shown. The only animal in which gravity has been definitely shown to be an important factor during growth is antennularia, and it has been found that gravity is also a factor in the regeneration of the same form. Not only is this influence shown in the growth of the new part that has developed, but the same influence seems to be one of the factors that determines where the new growth takes place. This latter relation is known in only a few cases, for instance in plants, according to Vöchting, and in antennularia, according to Loeb, so that, until further evidence is forthcoming, it is best not to extend this generalization too far; but it seems not impossible that it may be generally true. How an external factor may determine the location of new growth, as well as the subsequent development of the new part, we do not know at present.

In regard to the internal factors that influence the growth and the regeneration of new parts, we are almost completely in the dark. In cases of hypertrophy of the kidney, etc., the evidence seems to show that a specific substance, urea, that is normally taken from the blood by this organ may, if present in more than average amounts, excite the cells to greater activity and to growth, but whether the urea itself does this directly, or only indirectly through the greater functional activity of the cells, has not, as we have seen, been ascertained. That growth is influenced by internal factors can be shown, at least in certain cases, even although we cannot refer to the definite chemical or physical factors in the process. Some experiments that I have made on the tails of fish show very clearly the action of an internal factor. If the tail of fundulus is cut off obliquely, as indicated by the line 2–2 in Fig. 40, *A*, new material appears in a few days along the outer cut-edge. It appears to be at first equal in amount along the entire edge. As the material increases in width, it grows faster over

that part of the edge that is nearer the base of the tail (Fig. 40, *C*).
This growth continues to go on faster on the lower side, until the
rounded form of the tail is produced. If we make the oblique cut so
that the part nearer the base of the tail is on the upper side, the result
is the same in principle ; the upper part of the new material grows
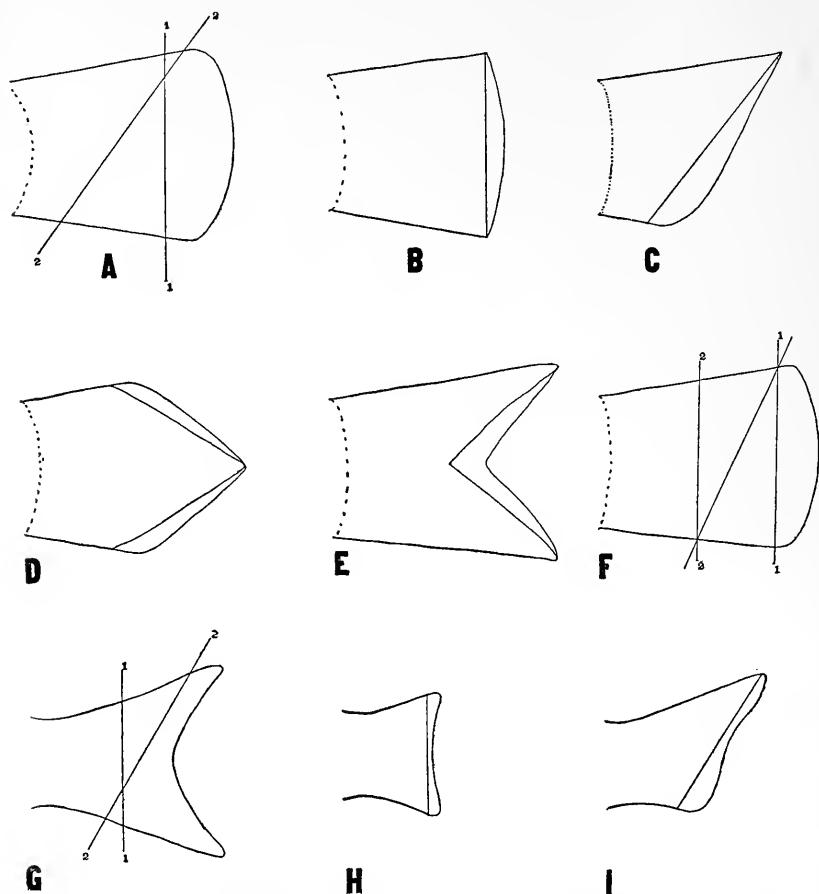faster than any other part. If we make two oblique cuts on the same



FIG. 40. — *A*. Tail of *Fundulus heteroclitus*. Lines indicate levels at which *B* and *C* were cut off.
*B*. Regenerating from cross-cut. *C*. Regenerating from oblique cut. *D*, *E*. Regenerating
from two oblique surfaces. *G*. Tail of stenopus. *H*, *I*. Tail of last cut off squarely and
obliquely.

tail, as shown in Fig. 40, *D*, or as in *E*, the new part grows
faster in each case on that part of the cut-edge that lies nearer the
base of the tail. These results may be supposed to be due to the better
nourishment of the new tissues nearer the base of the tail; but it is
not difficult to show that the difference in the rate of growth over
different parts of the cut-edge is not due to this factor. If, for

example, we cut off the tail of one fish squarely near the outer end, as shown in Fig. 40, *F*, 1–1, and the tail of a second near the base of the tail, as shown in Fig. 40, *F*, 2–2, and of a third by an oblique cut that corresponds to a cut extending from the upper side of the cut-edge of the tail of the first fish to the lower cut-edge of the tail of the second fish, as shown in Fig. 40, *F*, we find that the rate of growth over the first and second tails is about the same as that of the lower side of the third tail. In other words, the maximum rate of growth that is possible for the entire oblique edge is carried out only near the lower edge, and the growth of the rest of the new material is held in check. By means of another experiment a similar phenomenon can be shown. If the bifurcated tail of a young scup (*Stenopus chrysops*) is cut off by a cross-cut (Fig. 40, *G*, 1–1), it will be found that at first the new material is produced at an equal rate along the entire cut-edge; but it soon begins to grow faster at two points, one above and the other below, so that the characteristic swallow-tail is formed at a very early stage (Fig. 40, *H*) and before the new material has grown out to the level of the notch of the old tail. If the tail of another individual is cut off by an oblique cut (Fig. 40, *G*, 2–2), we find, as shown in Fig. 40, *I*, that at two points the new tail grows faster, but the lower lobe faster than the upper one.

These results show very clearly that in some way the development of the typical form of the tail influences the rate of growth at different points. The more rapid growth takes place in those regions at which the lobes of the tail are developing. In other words, although the physiological conditions would seem to admit of the maximum rate of growth over the entire cut-edge, this only takes place in those parts that give the new tail its characteristic form. The growth in other regions is held in check. The same explanation applies to the more rapid growth at that part of an oblique cut that is nearest the base of the tail, for by this means the tail more nearly assumes its typical form.

These results demonstrate some sort of a formative influence in the new part. We can refer this factor at present only to some structural feature that regulates the rate of growth. We find here one of the fundamental phenomena behind which we cannot hope to go at present, although it may not be beyond our reach to determine in what way this influence is carried out in the different parts. This topic will be more fully considered in a later chapter.

Another illustration may be given from certain experiments in the regeneration of *Planaria lugubris*. If the posterior end is cut off just in front of the genital pore, as indicated in Fig. 41, new material develops at the anterior cut-edge, and in a few days a new head is formed out of this new material. A new pharynx appears

in the new tissue immediately in front of the old part. It lies,
therefore, just behind the new head. The proportions of the new
worm are at this time very different from those of a typical worm,
since the head is much too near to the new pharynx and to the old
genital pore. New material is now produced in the region behind
the head and in front of the pharynx, so that the head is carried
further forward until the new worm has fully assumed the character-
istic proportions. As the new head is formed the old part loses its
material, so that it becomes flatter and narrower, and if the worm is
not fed the old part may lose also something of its former length.
If the worm is fed, however, as soon as the pharynx develops the
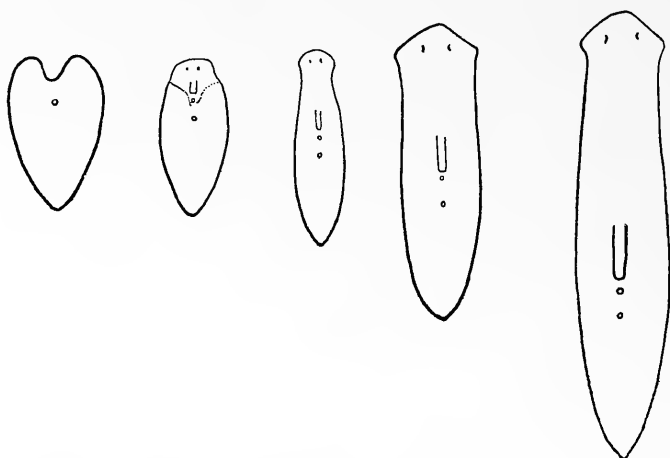old part loses less and the new part grows forward more rapidly.



FIG. 41. — Posterior end of *Planaria lugubris*, cut off between pharyngeal and genital pores.
Figure to left shows the piece after removal. The four figures to the right show the regenera-
tion of the same piece, drawn to scale. As soon as the new pharynx had developed, the
worm was fed. The experiment extended from November 17 to January 8.

The most striking phenomenon in the growth of the new worm is
the formation of new material in the region behind the head. The
result of this growth is to carry the head forward and produce the
characteristic form of the animal. This change is all the more in-
teresting since the growth does not take place at a free end, but in
the middle of the new material. It is only by the formation of new
material in this region that the head is carried to its proportionate dis-
tance from the pharynx. It appears that in some way the growth is
regulated by influences that determine the form of the new organism.
    Another experiment on the same animal gives also a somewhat
similar result. If a worm is cut in two obliquely (Fig. 21, *B*) and
the regeneration of the posterior piece is followed, it is found that
the new material appears at first evenly along the entire cut-surface.

It then begins to grow faster on one side (Fig. 21, *b*), and a head appears in this region with its axis at right angles to the cut-edge. As the head grows larger the growth is more rapid *on one side*, and as a result the head is slowly turned forward (Fig. 21, *b*). This more rapid growth on one side brings the new head finally into its typical position with respect to the rest of the piece. The end result of these changes is to produce a new worm having a typical form. If the oblique cut is made behind the old pharynx, as in Fig. 22, *A*, the new pharynx that appears in the new material along the cut-edge lies obliquely at first, indicating that the new median line is very early laid down in the new part, and connects the middle line of the old part with the middle of the new head. As the region behind the new head grows larger and broader the pharynx comes to lie more and more in an antero-posterior direction, and finally, when the new part is as broad as the old,[1] the pharynx lies in the middle line of a symmetrical worm.

These results show that the new growth may even take place more rapidly on one side of the structural median line than on the other, and on that side that must become longer in order to produce the symmetrical form of the worm. Here also we find that a formative influence of some sort is at work that regulates the different regions of growth in such a way that a typical structure is produced. The more rapid growth on one side is, however, in this case clearly connected with the relatively smaller development of the organs on that side, and perhaps this same principle may explain all other cases. If so the phenomenon appears much less mysterious than it does when the growth is referred to an unknown regulative factor.

### DOUBLE STRUCTURES

A structure that is single in the normal animal may become double after regeneration, and in some cases the special conditions that lead to the doubling have been determined. Trembley showed that if the head of hydra is split lengthwise into two parts, each part may.complete itself and a two-headed form is produced. If the posterior end of a hydra is split, an animal with two feet is made. It is true that the two-headed forms may subsequently separate after several weeks into two individuals, and even the form with two feet may lose one of them by constriction, as Marshall and King have shown. Driesch has produced a tubularian hydroid with two heads by splitting the stem partially into two pieces. Each head is perfect in all respects, and although each has fewer tentacles than

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[1] If the young worm is fed the new part becomes almost as broad as the old piece, but if the worm is not fed the old part decreases in breadth and the new part does not grow as broad as in the former case.

the head that regenerates from an undivided stem, yet the number of tentacles on each head is more than half the average number. This is connected apparently with the fact that the circumference of each half is greater than half the circumference of the original stem. Planarians with double tails, produced by partial splitting, have been described by Dugès and by Faraday, and it has also been shown that by partial splitting of the anterior end of the worm two heads can be produced. Van Duyne, Randolph, and Bardeen and I have obtained the same result. Each half completes itself on the cut-side and produces a symmetrical anterior end. If one of the heads is cut off, it will be again regenerated. If the heads are united very near to the trunk, as in Fig. 42, *A*, they may never grow to the full size of the
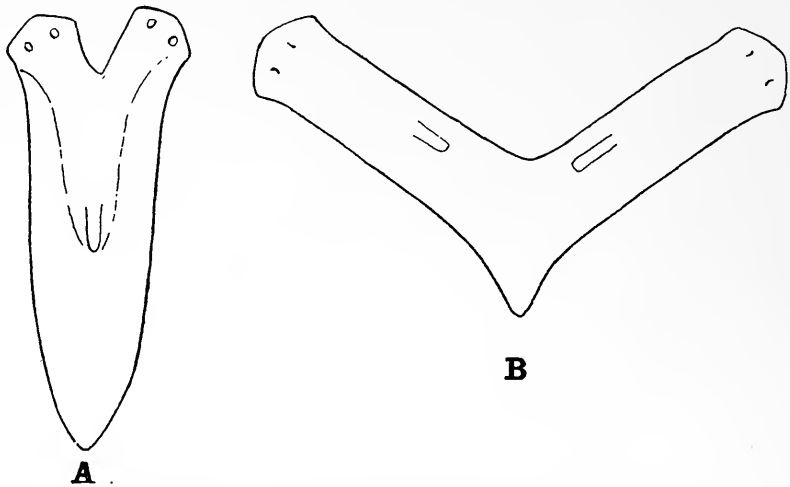


FIG. 42. — *Planaria lugubris*. *A*. Two heads produced after operation similar to that in Fig. 24. Each head about half size. *B*. Worm split in half through level of pharynx. New half-worms larger than half of normal worm.

original head, as I have found; but if the pieces have been split posteriorly, so that each head has a long anterior end, then each one may become nearly as large as the original head (Fig. 42, *B*). We see in these cases the influence of the region of union on the growth of the new part. If the new part is near the region of attachment, the smaller size of the latter restrains the growth of the new head; but if the region of union is farther distant, the head may grow more nearly to its full size despite the influence of the region of union. King has found in the starfish that if the arm is split lengthwise, each half may complete itself laterally and a forked arm result. An additional entire arm may be formed by splitting the disk partially in two between two arms. If the cut-edges do not reunite a new arm will grow out from each cut-surface (Fig. 38, *E*). In this case the de-

velopment of the new arm cannot be accounted for on the assump-
tion that the typical form completes itself, since a sixth arm cannot
be supposed to be a typical structure in the starfish. The result must
depend on other factors, such as the presence of an open surface in a
region where the cells have the power of making new arms.

Barfurth has been able to produce a double tail in the tadpole by
the following method: A hot needle is thrust into one side of the
tail, so that the notochord and the nervous system are injured. The
tail is then cut off just posterior to the region injured by the needle.
A new tail grows out from the cut-end, and also in some cases an-
other tail grows out at the side where the notochord was injured by
the needle. The injury to the notochord and the removal of tissue
immediately about it leads to a proliferation of cells, around which
other tissues are added and the new tail produced.

Lizards with double tails have often been described,[1] and it now
appears that all these cases are due to injuries to the normal tail.
Tornier has succeeded, experimentally, in producing double and
even triple tails. If the end of the tail is broken off, and the tail
is then injured near the end, two tails may regenerate, one from
the broken end and one from the region of injury (Fig. 43). Under
natural conditions this might occur if the tail were partially bitten off
and the end of the tail lost at the same time. A regenerated tail may
produce another tail if it is wounded. A three-tailed lizard may be
made by cutting off the tail and then making two injuries proximal
to the broken end. Two of the new tails may be included in the
same outer covering if they arise near together, as shown in Fig.
43, *B*. Lizards with two or three tails may be produced in another
way. If the tail is cut off very obliquely, so that two or three verte-
bræ are injured, there arises from each wounded vertebra a cartilagi-
nous tube that forms the axis of a new tail. Tornier thinks that
the regeneration is the result of overnourishment of the region where
the injury has been made, but this does not seem in itself a sufficient
explanation. Tornier has also been able to produce, experimentally,
double limbs in *Triton cristatus* in the following way: The limb is
cut off near the body, and, after the cut-end has formed new tissue,
a thread is tied over the end in such a way that it is divided into two
parts. As the new material begins to bulge outward it is separated into
halves by the constricting thread, and each part produces a separate
leg (Fig. 43, *D*). The soles of the two feet in the individual repre-
sented in Fig. 43, *D*, are turned toward each other. The femur is
bifid at its outer end, and to each end the lower part of one leg is
attached. The bones in this part are fused together at the knee, so
that only the foot portions can be separately moved.

[1] See Fraisse for literature.

The same method used to produce double tails in the lizard can also be used to produce double legs. The femur is broken in the vicinity of the hip-joint, and the soft parts are cut into over the break. Then, or better somewhat later, the leg is amputated below the
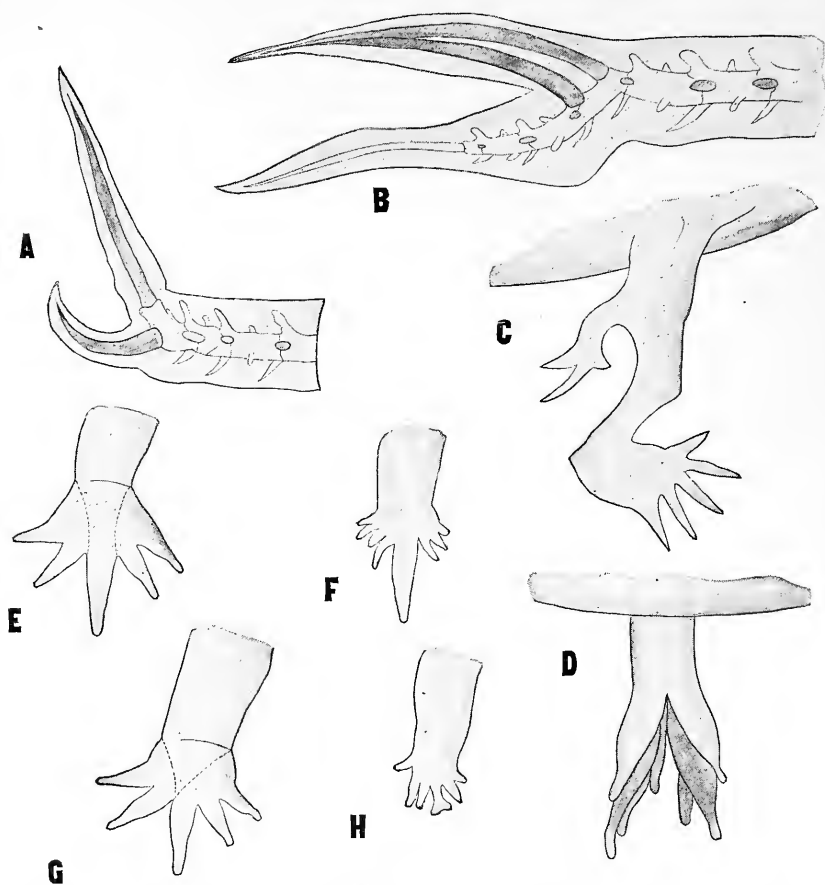


FIG. 43. — After Tornier. *A. Lacerta agilis*. Produced by partly breaking off old tail. New tail arises at place of breaking. Old tail also remains. *B.* Three-tailed form — two tails being united in a common covering. Old tail had been cut off (it regenerated the lower branch from cut-end) and two proximal vertebræ that had been injured. *C.* Additional limb of *Triton cristatus* produced by wounding femur. *D.* Double foot of *Triton cristatus* produced by tying thread over regenerating stump. *E.* Foot of *Triton cristatus*. Dotted lines indicating how foot was cut off. *F.* Regeneration of same. *G.* Another way of cutting off foot. *H.* Result of last operation.

broken part. A new limb regenerates from the cut-end, and at the same time another limb grows out from the broken femur (Fig. 43, *C*). The same result is reached if the femur has a slit cut into it in the region of the hip-joint, so that it is much injured. Later the leg is cut off below the place of injury. A double leg is the result.

Feet with supernumerary digits can also be produced by artificial wounds. If the first and second and then the fourth and fifth toes are cut off, as indicated by the lines in Fig. 43, *E*, so that a part of the tarsus and a part of the tibia and fibula are cut away (the third finger being left attached to the remaining middle portion), more toes grow out from the wounded surface than were removed, as shown in Fig. 43, *F*. A similar result may be obtained in another way. If the first and second toes are cut off by an oblique cut (Fig. 43, *G*), and then after the wound has healed the third, fourth, and fifth toes are also cut off by another oblique cut (a part of the tarsus being removed each time), more toes are regenerated than were cut off [1] (Fig. 43, *H*).

Tornier suggests that the double feet that are sometimes formed in embryos — even in the mammalia — have resulted from a fold of the amnion constricting the middle of the beginning of the young leg, in the same way as is brought about artificially by tying a string over the growing end of the regenerating leg of triton.

In many of these cases, in which the double structure is the result of splitting the part in the middle line, the completion of the new part is exactly the same as though the parts had been entirely separated. The only special problem that we meet with in these instances is that this doubling is possible while the piece remains a part of the rest of the organism. This shows that there is a great deal of independence in the different parts of the body in regard to their regenerative power, and that local conditions may often determine the formation of double structures.

It has been shown during the last decade that double embryos may be produced artificially by incomplete separation of the first two blastomeres. Driesch, Loeb, and others have demonstrated that if the first two cells of the egg of the sea-urchin be incompletely separated, each may produce a single embryo and the two remain sticking together. Wilson has shown in amphioxus that the same result occurs if the first two cells are partially separated by shaking. Schultze has shown in the frog that if at the two-cell stage the egg is held in an inverted position, *i.e.* with the white hemisphere turned upwards, each blastomere gives rise to a whole embryo — the two embryos being united, sometimes in one way, sometimes in another, as shown in Fig. 63. In this case it appears that the results are due to a rotation of the contents of each blastomere, so that like parts of the two blastomeres become separated. In the egg of the sea-urchin, and of amphioxus, gravity does not have a similar action on the egg, but the results seem to be due to a mechanical separation of the blastomeres. These cases of double structures, produced by the segmenting egg,

[1] In the figure one double or forked toe is present.

appear to belong to the same category as those described above for
adult forms—especially in those cases where pieces regenerate by
morphallaxis.

In connection with the production of double structures there
should be mentioned a peculiar method of formation of new heads,
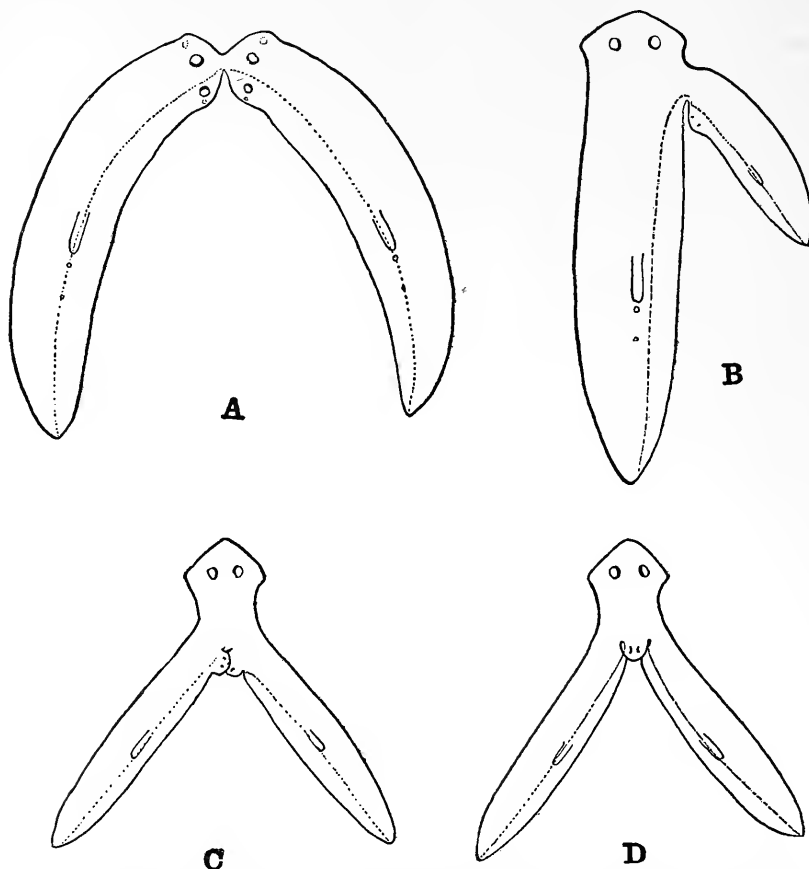first discovered by Van Duyne in a planarian. He found that if the



FIG. 44.—*A. Planaria lugubris,* cut in two as far forward as region between eyes, regenerating
half-heads. *B.* Same cut in two at one side of middle line. Smaller piece produced a new
head. *C. Planaria maculata,* split in two. It produced two heads in angle. *D.* Another,
that produced a single head in angle.

animal is cut in two in the middle line, the halves being left united
only at the head-end, as shown in Fig. 44, *D, C,* there may appear one
or two new heads in the angle between the halves. I have repeated
this experiment with the same result, and have found that it may also
occur when only a piece is partially split from the side of the body,
as shown in Fig. 44, *B.* In Van Duyne's experiment the two new

heads do not appear unless the cut extends far forward, but if the division extends into the region between the two eyes there may be formed, as I have found, a single eye on each side that makes a pair with the old eye of that side (Fig. 44, *A*). It is evident in this case that each head has completed itself on the cut-side, the completion including the eye and the side of the head also with its "ear-lobe." The result, in this case, is the same as though the pieces had been completely cut in two. If the cut does not extend quite so far forward there are usually formed one or two heads near the angle, each with a pair of eyes and a pair of ear-lobes (Fig. 44, *C*). Sometimes a single head develops in the angle itself (Fig. 44, *D*), and it is difficult to tell whether it belongs to one or to the other side, or whether it is common to both sides. Van Duyne spoke of the double and single head of the latter kind which he obtained as heteromorphic structures in Loeb's use of the term. According to this definition, heteromorphosis is the replacement of an organ by one that is morphologically and physiologically unlike the original one, but this statement has been made to cover a number of different phenomena. The examples of heteromorphosis that Loeb gives by way of illustration of the phenomenon are : the production of a hydranth on the aboral end of tubularia, and the formation of roots in place of a stem in antennularia, etc. The formation of the heads in the angle in planarians does not appear to me to belong in this category. It seems rather that the phenomenon is of the same sort as the formation of a new head at the side of a longitudinal piece, and if so the new heads in the angle are, therefore, in their proper structural position for new heads belonging to the posterior halves. Even if it should prove true that a single head may develop exactly in the angle itself, and belong to both sides, it can be interpreted by an extension of the same principle.[1] The position of this median head turned backward suggests an obvious comparison with the production of the heteromorphic head in *Planaria lugubris*, but a closer examination will show, I think, that the two cases are different. The heteromorphic head is produced only when the head is cut off close behind the eyes. If cut off slightly behind this region, a posterior end is generally formed. But in the worms split lengthwise the head in the angle may be formed at a level much farther posteriorly than the eyes. If the split extends into the head, then the eyes that develop are the supplements of those of the old part. Our analysis leads, therefore, to the conclusion that the heads, or parts of heads, in the split worms are not heteromorphic structures but supplementary heads.

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[1] A parallel case is found when a piece partially split in two at the anterior end (Fig. 24) produces one or two heads on each half, according to the extent of fusion of the new material that goes to form the new head or heads.

# CHAPTER VIII

## SELF–DIVISION AND REGENERATION. BUDDING AND REGEN-
## ERATION. AUTOTOMY. THEORY OF AUTOTOMY

SELF-DIVISION, as a means of propagation, is of widespread occur-
rence in the animal kingdom. In some cases the animal simply
breaks into pieces and subsequently regeneration takes place in the
same way as when the animal is cut into pieces by artificial means.
In other cases the parts are gradually separated, and during this
time new parts are formed by a process resembling that of regenera-
tion after separation. A few zoologists have tried to show how the
process of regeneration before separation has been derived from
regeneration following self-division. It is our purpose to examine
here the evidence in favor of this hypothesis.

A study of the forms that propagate by means of self-division
shows that the process is present in many groups of the animal
kingdom. In the unicellular forms this method is universally present;
and in the multicellular forms the division of the individual cells is
looked upon as a process similar to the method of propagation in the
protozoa. The sponges do not multiply by self-division. In the
cœlenterates, on the other hand, we find this mode of propagation
present in most forms. Hydra appears rarely, if at all, to divide by
a cross-division, and, although one or two cases of longitudinal
division have been described, it is not improbable that they have
been started by the accidental splitting of the oral end. The hydro-
medusæ, *Stomobrachium mirabile*, *Phialidium variabile*, *Gastroblasta
Raffælei*, are known to increase by division.[1] Several actinians and
many corals divide longitudinally, while the scyphistoma of the
scyphomedusæ produce free-swimming ephyras by cross-divisions
of the fixed strobila stage. The ctenophors do not divide.

It is known that several fresh-water planarians propagate by
division, the tail-end breaking off in the region behind the old
pharynx. In one form,[2] and possibly in others, regeneration may
begin before the separation takes place. Many of the rhabdocœ-
lous planarians increase by cross-division — the separation taking
place more nearly in the middle of the body. In these forms the

[1] See Lang ('88).     [2] See Zacharias ('86).

parts develop new organs more or less completely before they separate. In the trematodes self-division does not take place. The division of the body of the tapeworm into proglottids may represent a process of self-division, but the proglottids do not regenerate after separation.

The nemertians break up readily into pieces, if roughly treated or if the conditions of life are unfavorable, but this can scarcely be spoken of as a process of voluntary self-division. Regeneration takes place in some species, but imperfectly or not at all in others.

In the group of annelids we find many cases of self-division, especially in marine polychætes and in fresh-water oligochætes. One of the most interesting forms, belonging to the first group, is the palolo worm in which the swimming headless form, that is set free by division, serves to distribute the sexual products. Subsequently it appears that the piece dies without regenerating a new head. If we examine more in detail some of the cases of self-division in annelids, we find the following interesting facts. In nereis the posterior region of the body undergoes great changes of structure, the new worm being known under a different name, viz. heteronereis. In this part of the worm, eggs (or sperm) are produced, but it does not separate from the anterior end as a distinct individual. In the family of scyllids the changes that take place in the posterior or sexual end of the body are often accompanied by non-sexual modes of fission. In some species the changes that take place are like those in nereis, and no separation occurs; in other species the sexual region becomes separated from the anterior or non-sexual regions. In scyllis a new head develops, *after separation*, on the sexual or posterior piece. A new tail is also regenerated by the non-sexual or anterior piece, and as many new segments are formed as are lost. The new posterior region may again produce sexual cells, and again separate. In autolytus a new head develops on the posterior piece *before it separates*. A region of proliferation is also found at the posterior end of the anterior part. In some species new individuals develop in this zone of proliferation, and a chain of as many as sixteen worms may be present before the one first formed drops off. A still more complicated process is found in myriana. The region just in front of the anus elongates, and gives rise to a large number of segments. These form a new individual with the head at the anterior end. Then another series of segments is proliferated at the posterior end of the old, or anterior worm, and just in front of the first-formed individual. This region also makes a new individual. The process continuing, a chain of individuals is produced, with the oldest individual at the posterior end and the youngest at the anterior end of the series. Each individual grows larger, and produces

more segments at its posterior end.   Reproductive organs appear in each individual, and when the germ-cells are mature the chain breaks up.

None of the earthworms propagate by self-division, although occasionally, under unfavorable conditions, pieces may pinch off at the posterior end.[1]   Lumbriculus, on the other hand, propagates by self-division, although it has been disputed whether the division takes place without the intervention of an external injury or disturbance of some sort, or whether the division may take place entirely from internal causes, that is, spontaneously.   Von Wagner has shown that at certain seasons lumbriculus breaks up much more readily than at other times, which may only mean that it is more sensitive to stimuli at one time than at another.

The pieces into which lumbriculus breaks up regenerate after separation.   In another form, *Ctenodrilus monostylos*, division takes place first in the middle of the body behind a cross-septum.   Each half may again divide in the same way, and the same process may be repeated again and again until some of the pieces are reduced to a single segment.   A new anterior and posterior end may then develop on each piece.   In *Ctenodrilus pardalis* each segment of the middle region of the body constricts from the one in front and from the one behind, and each produces a new head at its anterior end and an anal opening at its posterior end.   The worm then breaks up into a number of separate worms.   In this series, self-division of the individual is not associated with the development of sexual forms, but seems to be a purely non-sexual method of reproduction.   In the leeches self-division does not occur, and no cases are known in the mollusks.

In the echinoderms several forms reproduce by voluntary self-division.   In the brittle-stars some forms divide by the disk separating into two parts, one having two and the other three of the old arms. Each piece of the disk then regenerates the missing part of the disk as well as the additional arms.   In the starfishes the arms may be thrown off if injured, and, while in certain forms the lost arm does not regenerate a new disk, yet, according to several writers, it may in other species regenerate a new animal.   Dalyell observed a process of self-division in a holothurian, each part producing a new individual, and more recent observers have confirmed this discovery.

No cases of self-division are known in the groups of myriapods, insects, crustaceans, spiders, polyzoans, brachiopods, enteropneusta, or vertebrates.

Before discussing the general problems connected with the preceding cases, I should like to point out that it is certainly a striking fact that in all, or nearly all, of these cases of self-division, the sepa-

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[1] See Hescheler ('97).

ration takes place in the shortest axis, without regard to the structure of the animal. A law similar to that enunciated in connection with the division of the cell seems to hold for the organism as a whole : namely, division takes place, as a rule, in the shortest diameter of the form. The protozoa are, in a sense, excluded, since being unicellular forms they come under the rule for the division of the cell. In the cœlenterates we find the actinians and corals, that have short, cylindrical bodies, dividing from the oral to the aboral end, while the longer scyphistoma divides transversely. The flat, bell-shaped medusa, gastroblasta, divides in an oral-aboral plane. The flat-worms and annelids divide transversely, and, therefore, in the plane of least resistance. The most important illustrations of this principle are furnished by the echinoderms. Those brittle-stars that divide through the disk do so in the shortest direction, that is, from the oral to the aboral side, whilst the holothurians that are long, cylindrical forms divide across the body and, therefore, in a structural plane at right angles to that of the brittle-stars. It may be claimed that in all these cases the plane of division is that in which the animal is most likely to be broken in two by external agents, but this is, I think, only a coincidence, and the result is really due to internal conditions. The division is brought about in most cases, and perhaps in all, by the contraction of the muscles ; and the arrangement of the muscles in connection with the form of the body is the real cause of the phenomenon.

Returning to the general question of the occurrence of the process of division in the different groups, we find that in nearly all of them in which self-division occurs it is found in a number of different forms in the same group. The process seems to be characteristic of whole groups rather than of species, and so far as evidence of this sort has any value it points to the conclusion that the process is not necessarily a special case of adaptation to the surroundings, because the species that divide may live under very diverse conditions.

A further examination of the facts throws a certain amount of light on the relation between the processes of self-division and of regeneration. The following questions may serve to guide us in our examination :—

(i) Is regeneration found only in those groups in which self-division takes place as a means of propagation ; or, conversely, does self-division only occur in those groups that have the power of regeneration ?

(ii) Is regeneration confined, in the groups that make use of self-division as a means of propagation, to those regions of the body where the self-division takes place ?

(iii) Is regeneration as extensive in the groups that do not propagate by self-division as in those that do ?

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(iv) Can we account, in any way, for the presence of self-division in certain groups, and for its absence in others?

(v) What relation exists between the forms that prepare for subsequent self-division and those that do not?

The first question is easily answered. Regeneration is also found in nearly all the other groups that do not propagate by self-division, —as, for instance, the mollusks, vertebrates, etc. The second half of the question may also be answered. All the groups that propagate by self-division have also the power of regeneration.[1]

In answer to the second question there is ample evidence showing that regeneration is by no means confined to those regions of the body in which the self-division occurs.

In answer to the third question, it may be stated that although, in the groups that propagate by self-division, regeneration may be present in nearly all parts of the body, the same phenomenon occurs in other groups that do not propagate by division.

The fourth question offers many difficulties, and our answer will depend largely upon what we mean by *"accounting for"* the process in certain groups. If the question is interpreted to ask, Why does an animal divide? no answer can be given. If it is meant to ask, Can we see how the process would be difficult, or even impossible, in certain groups and not in others? then an approximate answer may be given, or at least an hypothesis formed. In the first place, the power of regeneration must be present in the region at which the self-division takes place in order that the result may lead to the formation of new individuals, or else be acquired in that region along with the acquirement of the means for division. A leech is not much more complicated than a marine annelid, yet it has little or no power of regeneration; hence, perhaps, propagation by division could not be acquired by the leeches until they had first acquired the power to regenerate. In the second place, in certain forms a separation of the body into two parts would lead to the death of one or of both parts, owing to the dependence of the different regions upon each other. In forms like the vertebrates, insects, crustacea, etc., we can readily see why this would be the case. Hence propagation by means of self-division could not be acquired, since the division itself would lead to the destruction of the organism. In the third place, the structure of the body may be such that the process of self-division would be mechanically impossible. A hard outer coat, like that of the sea-urchin, combined with a weak development of the mus-

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[1] The proglottids of the cestodes seem to be an exception, but they are little more than sacs filled with embryos at the time of their separation. How far regeneration may take place in the scolex, or young proglottids, is not known, but it is not improbable that some of the abnormal forms that have been described may be due to regeneration.

culature of the body, would effectively prevent the self-division of the animal.

The fifth question has many sides. It involves us on the one hand in a historical question of the origin of self-division, and on the other hand in a discussion of the stimulus that brings about, not only the division, but the changes that precede the division in those cases in which the new part develops before division takes place.

Several zoologists have held that the process of self-division followed by regeneration has been the starting-point for the process of propagation preceded by regeneration. Von Kennel, for instance, maintains that self-division in some of the annelids has arisen in this way. He says: "We recognize everywhere in the animal kingdom the power of organisms to replace lost parts, and we call this regeneration. It may be developed in very different degrees in animals, and, as a rule, only those parts of the body have the power of regeneration that still possess the organs that are essential for independent existence. The higher the organization of the animal, so much the less is its power of regeneration, perhaps, because the division of labor of the different organs has gone so far that extensive injuries cannot be repaired. . . . There is no doubt that this power is adaptive, in a high degree, to preserve the species under unfavorable conditions, so that they are much better off in the battle for existence than are the animals that live under the same conditions but have not the power of regeneration. . . . The power of regeneration that gives the animal a better chance in the battle for existence and, therefore, makes more certain the continuance and the distribution of the species will be, as is well known from numerous observations, in a high degree inherited, indeed even increased so that its descendants will possess that power in a higher degree than their forefathers; and, in consequence, a much smaller stimulus (motive) suffices, than at first, to bring about the division of the parts." After showing, according to the usual formula, that the process of regeneration is useful, and, *therefore*, would come under the guidance of natural selection, von Kennel proceeds to show how the result is connected with an external stimulus! He asks: "Can accidental injuries account for the result (viz. for the division in lumbriculus, planarians, and starfish), since how few starfish are there with regenerating arms in comparison with the enormous number of uninjured individuals? Should we not rather look for the external stimuli that have initiated the process of self-division?" "Animals that have developed the power of regeneration by a long process of inheritance will have acquired along with this the property of easier reaction to all external adverse conditions. In a sense the sensitiveness for such stimuli is sharpened, and the animal responds at once by breaking up. In the same way the

ear of a good musician becomes more sensitive through practice. If we think of the same stimulus as regularly recurring, and as always answered in the same way, then we may look upon it as a normal condition of the life of the animal and its response as also a normal process in the animal. If, for instance, the breaking into pieces of lumbriculus is a consequence of the approach of cold weather or of other external conditions, then the organization of this animal must react by breaking up in consequence of its adaptation to the conditions acquired through heredity. The self-division becomes a normal process under normally recurring conditions. If the organism has been accustomed to respond through numerous generations, and, therefore, its sensitiveness has become highly developed, it will be seen that it may be influenced by the slightest change in the unfavorable conditions, and although, at first, the change may not be sufficiently strong to cause the animal to divide, yet the introductory changes leading to the division may be started, which will in turn make the division, when it occurs, easier and the animal that possesses this responsiveness more likely to survive. This would be the case if a slow process of constriction took place, so that, at the time of separation, no wounds of any size are formed." "By a further transfer of the phenomenon, a partial, or even a complete, regeneration may set in before division takes place." "We find changes like this in the series of forms, *Lumbriculus*, *Ctenodrilus monostylos*, *Ctenodrilus pardalis*, *Nais*, *Chætogaster*. It appears in a high degree probable that the series has originated in the way described. Perhaps zoologists will find after some thousands of years that lumbriculus propagates as does nais at present." In this way von Kennel tries to show how the process of regeneration, that takes place before division, has been evolved from a simple process of breaking up in response to unfavorable conditions. The imaginary process touches on debatable ground, to say the least, at every turn, and until some of the principles involved have been put on a safer basis, it would be unprofitable to discuss the argument at any length.

We should never lose sight of the fact that the arranging of a series like that beginning with lumbriculus and ending with chætogaster is a purely arbitrary process and does not rest on any historical knowledge of how the different methods originated or how they stand related, and no one really supposes, of course, that these forms have descended from each other but at most that the more complicated processes may have been at first like those shown in other forms. Even this involves assumptions that are far from being established, and it seems folly to pile up assumption on top of assumption in order to build what is little more than a castle in the air.

## REGENERATION AND BUDDING

In several groups of animals a process of budding takes place that presents certain features not unlike those of self-division. It is difficult, in fact, to draw a sharp line between budding and self-division, and although several writers have attempted to make a distinction between the two processes, it cannot be said that their definitions have been entirely successful. It is possible to make a distinction in certain cases that may be adopted as typical, but the same differences may not suffice in other cases. For instance, the development of a new individual at the side of the body of hydra is a typical example of budding, while the breaking up of lumbriculus or of a planarian into pieces that form new individuals is a typical example of division. In a general way the difference in the two processes involves the idea that a bud begins as a small part of the parent animal, and increases in size until it attains a typical form. It may remain permanently connected with the parent, or be separated off. By division we mean the breaking up of an organism into two or more pieces that become new individuals, the sum-total of the products of the division representing the original organism. Von Kennel first sharply formulated this distinction, and it has been also supported by von Wagner, who has attempted to make the distinction a hard and fast one;[1] but as von Bock has pointed out, there are forms like pyrosoma and salpa in which the non-sexual method of propagation partakes of both peculiarities, and in *Syllis ramosa* the individuals appear to bud from the sides, while in other annelids a process of division takes place. Von Bock assumes, therefore, as more probable, that budding and self-division are only different phenomena of the same fundamental process. It might be better, I think, to go even further in order to clear this statement from a possible historical implication, and state only that the two processes involve some of the same factors.

Budding occurs in several groups of the animal kingdom. There are numerous cases in the protozoa, such, for instance, as that in noctiluca. In the sponges buds are formed that go to build up a colony in most instances. In the cœlenterates cases of lateral budding are found in nearly all the main groups, and in one and the same individual, as in the scyphistoma of aurelia, in fact both budding and division occur. In the polyzoa, in the ascidians, and in cephalodiscus lateral budding takes place. In the rhabdocoel turbellarians, and in some of the annelids, we find chains of new individuals produced by a process that is often spoken of as budding. It is convenient, however, to distinguish these cases of axial budding from those of lateral

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[1] Except for the protozoa.

budding; for, while they both involve an increase in the products over that of the original animal, the axial relations in lateral buds are established in a new plane, while in axial budding the main axis of the new animal is a part of that of the old, and this difference may involve different factors. The process of budding does not occur in the insects, spiders, crustaceans, mollusks, ctenophores, brachiopods, nematodes, vertebrates, or in several other smaller groups.

This examination shows that there are groups in which both processes take place, viz. cœlenterates, planarians, annelids; and others in which budding alone takes place, viz. ascidians, polyzoa, cephalodiscus; and one group at least in which division, but not budding, takes place, the echinoderms. It is obvious that from the occurrence of the process of budding in the animal kingdom we cannot infer anything as to its relation to division or to regeneration.

It has been pointed out that in the flowering plants, in which the growth takes place by means of buds, the power of terminal regeneration is very slightly developed, and its absence is sometimes accounted for on the ground that the new growth takes place by means of the development of lateral buds. If by this statement it is meant that buds being present the suppression of regeneration in other regions may occur, then there may be a certain amount of truth in the statement. If, however, it is intended to mean that *because* a plant has acquired the power of reproducing new parts by means of buds it has, therefore, lost the power to regenerate in other ways (or has never developed the power to regenerate), then the argument is, I think, fallacious; for we find even in flowering plants that the new buds sometimes arise from the new part, or callus, that forms over the cut-end, and this process resembles a real regenerative process. We also find that hydroids that produce lateral buds also regenerate freely from an exposed end. But we are at present so much in the dark in regard to the causes that bring about budding in organisms that a discussion of the possibilities would hardly be profitable.

<center>*AUTOTOMY*</center>

The process of autotomy differs only in degree from the process of self-division. In autotomy the part thrown off does not produce a new animal. The breaking off of the tail of the lizard at the base, if the outer part is injured, is an example of a typical process of autotomy. The throwing off of the crab's leg, if the leg is injured, is also another typical case of autotomy. There is a definite breaking-joint at the base of the crab's leg at which the separation always takes place (Fig. 45, A I–I). The breaking-joint is in the middle of the second segment from the base of the leg, where there is found,

on the outside of the leg, a ring-like groove that marks the place of rupture. A comparison of the legs of the crab with the walking legs of the crayfish, or of the lobster, shows that the groove in the crab's legs corresponds to a joint in the legs of the two other forms. In the crayfish and lobster the walking legs generally break off at this same level, although by no means as easily or with as much certainty as in the crab. The first pair of legs of the crayfish and
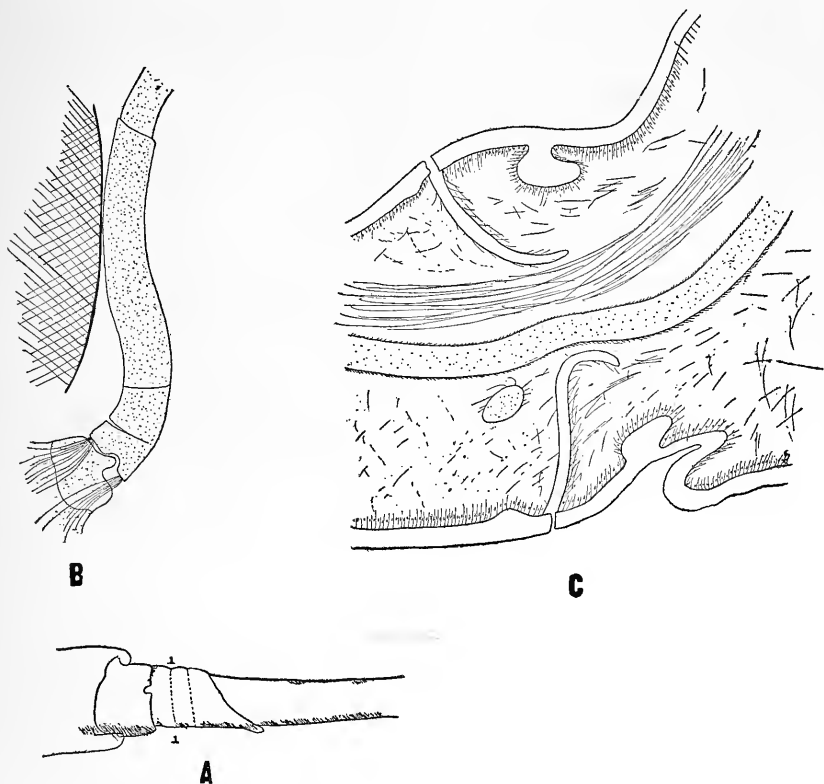


FIG. 45.—*A.* After Andrews. Base of leg of crab to show breaking-joint, 1–1. *B.* After Fredericq. Diagram of leg of crab to show how autotomy takes place. *C.* After Andrews. Longitudinal section of base of leg to show in-turned chitinous plate at breaking-joint.

lobster, carrying the large claws, have also a breaking-joint at the base of the leg similar to that in the crab's leg, and these legs break off in the living animal always at the breaking-joint.

Réaumur first recorded that if the leg of a crayfish or of a crab is cut off outside of the breaking-joint it is always thrown off later at the breaking-joint. Fredericq has made a careful examination of the way in which the leg is thrown off in the crab, *Carcinus mœnas.* He found that the breaking does not take place at the weakest part

of the leg; for the leg of a dead crab will support a weight of $3\frac{1}{2}$ to 5 kilograms, which represents about one hundred times the weight of the crab's body. When the weight is increased to a point at which the leg breaks, it does so between the body and the first segment or between the first and second segments. When it breaks off in this way, the edges are ragged and are left in a lacerated condition; but when the leg is thrown off by the animal at the breaking-joint, there is left a smooth surface covered over, except in the centre, by a thin cuticle. Through the opening in the centre of this cuticle a nerve and a blood vessel pass to the distal part of the leg. Very little bleeding takes place when the leg is thrown off, but if the leg is cut off or broken off at any other level the bleeding is much greater. Fredericq studied the physiological side of the process and found that it is the result of a reflex nervous act. He found that if the brain of the animal is destroyed the leg may still be thrown off, but if the ventral cord is destroyed the reflex action does not take place. The reflex is brought about ordinarily by an injury to the leg that starts a nerve impulse to the ventral nerve-cord, and from this a returning impulse is sent to the muscles of the same leg, causing the muscles in the region of the breaking-joint to contract violently, and the result of their contraction is to break off the leg. If the muscles are first injured, the leg cannot be thrown off. Andrews, who has studied the structure of the breaking-joint in the spider-crab, has found that there is a plane of separation extending inwards from the groove on the surface. This plane is made by a narrow space between two chitinous membranes that are continuous at their outer ends with the general chitinous covering of the leg (Fig. 45, *C*). When the leg breaks off, one-half of the double membrane is left attached to the base of the leg and the other to the part that is lost. This in-turned membrane seems to correspond to the in-turning of the surface cuticle in the region of the joints. The arrangement of the muscles at the breaking-joint is shown in Fig. 45, *B*. The upper muscle is the extensor muscle of the leg, and through its contraction the breaking off takes place. When it contracts the leg is brought against the side of the body, which is supposed to offer the resistance necessary to break off the leg. If the leg is held by an enemy, this may offer sufficient resistance for the muscle to bring about the breaking.

In many crabs the leg is not thrown off if simply held, but only after an injury. Even the most distal segment may be cut off and the leg remain attached, and sometimes it is not lost after the distal end of the next to the last segment is cut off. If a crab is tethered by one leg it will not throw off its leg in order to escape, unless, in the crab's excitement, the leg is twisted or broken. How generally

this holds for all crabs cannot be stated. Herrick says: " Unintentional experiments in autotomy have often been made by tethering a lobster or a crab by its large claws. The animal, of course, escapes, leaving only its leg behind. When lobsters are drawn out of the water by the claws, or when a claw is pinched by another lobster, or while they are handled in packing, especially for the winter market, they often ' cast a claw,' and the transportation of lobsters at this season is said to be attended by considerable loss in consequence." The large claws of the lobster are quite heavy, the base relatively small at the breaking-joint, and it may be that simply the weight of the claw, when out of the water, may strain the leg so that it breaks off, — the leg being injured by its own weight. The lobster seems to lose its claws quite often under natural conditions. Rathburn[1] states that "out of a hundred specimens collected for natural history purposes in Narragansett Bay in 1880, fully 25 per cent had lost a claw each, and a few both claws." Herrick[2] records that "in a total of 725 lobsters captured at Woods Holl in December and January, 1893–1894, fifty-four, or 7 per cent, had thrown off one or both claws."

The autotomy of the arms of the starfish has been often observed.[3] The arms are thrown off very near the base in many forms. If the animal is simply held by the arm it does not break off, but if injured it constricts and falls off. The lost arm does not regenerate a new starfish in most forms, but, as stated on page 102, there are recorded some cases in which the arm seems to have this power. King has found that out of a total of 1914 starfish (*Asterias vulgaris*) there were 206, or 10.76 per cent, that had new arms, and all of these, with one exception, arose from the base of the arm. The growth of the new arm from the base takes place more rapidly, as shown in Fig. 38, *A*, than when the arm is regenerated from a more distal level; but in the latter case the arm, despite its slower growth, may complete itself before another does that originates at the same time from the base of the old arm. There is, therefore, in this respect no obvious advantage, so far as regeneration is concerned, in throwing off the injured arm nearer to the disk.

In the brittle-stars (ophiurians) the arm breaks off with greater ease and at any level. If the arm is simply held and squeezed, it will, in some forms, break off just proximal to where it is held. If the broken end is again held, another small piece breaks off, and in this way the arm may be autotomized, piece by piece, to its very base.

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[1] *The Fisheries and Fishing Industries of the United States*, Washington, 1887.

[2] "The American Lobster," *Bull. U. S. Fish Comm.*, 1895.

[3] Réaumur in 1742 records the first observations. Spallanzani also described the process, and many later writers have examined it.

Regeneration may take place from any region, but, as yet, no observations have been made on the relative rate of growth of the new arm at different levels.

One of the most remarkable cases of autotomy is that in holothurians, in which the Cuvierian organs, and even the entire viscera, may be ejected when the animal is disturbed. A new digestive tract is regenerated.[1]

It is known that several of the myriapods lose their legs at a definite region near the base, and that they have the power of throwing off the leg in this region if it is injured. I have often observed that the legs of *Scutigera forceps* are thrown off if they are held or injured, and even when the animal is thrown into a killing fluid. Amongst the insects the plasmids or walking-sticks also throw off their legs at a definite joint, as described by Scudder, and more recently by Bordage, and still later by Godelmann. New legs are regenerated from the stump of the old leg, as has long been known.[2] Other insects do not have the power of throwing off their legs, and we have only a few observations that show that the legs if lost can be regenerated. It is known in the cockroach that the tarsus can regenerate if lost or if cut off, and that fewer segments are regenerated than are present in the normal animal. Newport found that the true legs of a caterpillar are regenerated during the pupa stage if they have been previously cut off.

A further example of autotomy is found in the white ants, which break off their wings at the base after the nuptial flight. There exists a definite and pre-formed breaking-plane in this region. The true ants also lose their wings after the nuptial flight, but there does not seem to be a definite plane of breaking, so that the process can scarcely be called one of autotomy. These cases also differ from the other cases of autotomy in that the lost parts are not renewed.

It has been observed[3] that if the leg of tarantula is cut off at any other place than at the coxa, the animal bites off the wounded leg with its jaws down to the coxa. In other spiders this does not occur, although Schultz has observed that when the legs are lost under natural conditions they are found broken off in most cases at the coxa. Schultz has also found that the legs regenerate better from this region than from any other. It would be rash, I think, to conclude without further evidence that the habit of tarantula to bite off a wounded leg down to the coxa has been acquired in connection with the better regeneration of the leg at this place. It is possible that the injury may excite the animal to bite off the leg as far as possible, which might be to the coxal joint. It would certainly be very remark-

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[1] The phenomenon has been observed by Dalyell, Semper, Minchin, and others.

[2] Müller, *Elements of Physiology*, 1837.          [3] By Wagner ('87).

able if this spider had acquired the habit in connection with the better regeneration of the leg at the base, since the leg can presumably also regenerate at any level, as in the epeirids.

In this same connection I may record that in the hermit-crab I have often observed that when a leg is cut off outside of the breaking-joint, if the leg is not thrown off at once, the claws of the first legs catch hold of the stump and, pulling at the leg, offer sufficient resistance for the leg to break off at the breaking-joint. I cannot believe that this instinct has anything to do with the better regeneration of the leg at the coxal joint, however attractive such an hypothesis may appear.

### THEORIES OF AUTOTOMY

A number of writers have pointed out that under certain conditions it is an obvious advantage to the animal to be able to throw off a portion of the body and thereby escape from an enemy. It has been suggested that if a crab is seized by the leg, the animal may save its life at times at the expense of its leg; and since the crab has the power of regenerating a new leg, it is the gainer in the long run by the sacrifice. The holothurian, that ejects its viscera, has been supposed to offer a sufficient reward to its hungry enemy, and escapes paying the death penalty, at the expense of its digestive tract. Thus, having shown that the process of autotomy is a useful one, it is claimed that it must have been acquired through a process of natural selection! An equally common opinion is that autotomy is an adaptation for regeneration, since in certain cases, as in that of the crab's leg, better conditions for subsequent regeneration occur at the breaking-joint than when the amputation takes place at any other region. Since less bleeding takes place when the crab's leg is thrown off at the breaking-joint, and since the wound closes more quickly when the arm of the starfish is lost at the base, it is assumed that we have in both cases an adaptation to meet accidents, and that the adaptation has been acquired by natural selection.

A consideration of these questions involves us once more in a discussion of the theory of natural selection. An attempt has been made in another place (pages 108–110) to show that we are not justified in assuming that because a process is useful, therefore it must have been acquired by means of natural selection. Even if it were granted that the theory of natural selection is correct, it does not follow that all useful processes have arisen under its guidance. We may, therefore, leave the general question aside, and inquire whether the process of autotomy could have arisen through natural selection (admitting that there is such a process, for the sake of the present argument), or whether autotomy must be due to something else.

If we assume that the leg of some individual crayfishes or crabs, for example, broke off, when injured, more easily at one place than at another, and that regeneration took place as well, or even better, from this region than from any other, and if we further assume that those animals in which this happened would have had a better chance of survival than their fellows, then it might seem to follow that in time there would be more of this kind of animal that survived.   But even these assumptions are not enough, for we must also assume that this particular variation was more likely to occur in the descendants of those that had it best developed, and that amongst those forms that survived, some had the same mechanism developed in a still higher degree, and, the process of selection again taking place, a further advance would be made in the direction of autotomy.   This, I think, is a fair, although brief, statement of the conventional argument as to how the process of natural selection takes place.   But let us look further and see if the results could be really carried out in the way imagined, shutting our eyes for the moment to the number of suppositions that it is necessary to make in order that the change may occur.   It will not be difficult, I believe, to show that even on these assumptions the result could not be reached.   In the first place, the crabs that are not injured in each generation are left out of account, and amongst these there will be some, it is true, that have the particular variation as well developed as the best amongst those that were injured, and others that have the average condition, but there will be still others that have the possibilities less highly developed, and the two latter classes will be, on the hypothesis, more numerous than those in the first class.   The uninjured crabs will also have an advantage, so far as breeding and resisting the attacks of their enemies are concerned, as compared with those that have been injured, and in consequence they, rather than the injured ones, will be more likely to leave descendants.   Even if some of those that have been injured, and have thrown off the leg at the most advantageous place, should interbreed with the uninjured crabs, still nothing, or very little, can be gained, because, on Darwinian principles, intercrossing of this sort will soon bring back the extreme variations to the average.

The process of natural selection could at best only bring about the result provided all crabs in each generation lose one or more of their legs, and amongst these only the ones survive that break off the leg at the most advantageous place; but no such wholesale injury takes place, as direct observation has shown.   At any one time only a small percentage, about ten per cent, have regenerating legs, and as the time required completely to regenerate a leg, even in the summer, is quite long, this percentage must give an approximate idea of

the extent of exposure to injury. It is strange that those who assert off-hand that, because autotomy is a useful process, therefore it must have been acquired by natural selection, have not taken the pains to work out how this could have come about. Had they done so, I cannot but believe they would have seen how great the difficulties are that stand in the way.

A further difficulty is met when we find that each leg of the crab has the same mechanism. If we reject as preposterous the idea that natural selection has developed in each leg the same structure, then we must suppose that a crab varies in the same direction in all its legs at the same time; and if this is true it is obvious that the principle of variation must be a far more important factor in the result than the picking out of the most extreme variations. The same laws that determine that one individual varies in a useful direction farther than do other individuals may, after all, account for the entire series of changes. If it be replied that natural selection does not take into account the causes of the differences of individual variation, this is to admit that it avowedly leaves out of account the very principles that may in themselves, and without the aid of any such supposed process as natural selection, bring about the result. The Lamarckian principle of use and disuse does not give an explanation of autotomy, since the region of the breaking-joint is not the weakest region of the leg, or the place at which the leg would be most likely to be injured.

We cannot assume autotomy to be a fundamental character of living things, since it occurs only under special conditions, and in special regions of the body. While it might be possible to trace the autotomy of the legs of the crustacea, myriapods and insects, to a common ancestral form, yet this is extremely improbable, because the process takes place in only a relatively few forms in each group. The autotomy of the wings of white ants that takes place along a preëxisting breaking-line must certainly have been independently acquired in this group. The breaking off of the end of the foot in the snail helicarion is also a special acquirement within the group of mollusca.

Bordage has suggested that the development of the breaking-joint at the base of the leg of phasmids has been acquired in connection with the process of moulting. He has observed that during this period the leg cannot, in some cases, be successfully withdrawn through the small basal region; and hence, if it could not break off, the animal would remain anchored to the old exoskeleton. It escapes at the expense of losing its leg. The animal, having acquired the means of breaking off its leg under these conditions, might also make use of the same mechanism when the leg is held or injured, and thereby escape its enemy. The fact that the crayfish has a breaking-joint only for the large first pair of legs would seem to be in favor of this interpre-

tation, but the crab has the same mechanism for the slender walking legs, that one would suppose could be easily withdrawn from the old covering.   It should also be remembered that we do not know whether the breaking-joint at the base of the leg of the crab and of the crayfish would act at the time when the leg is being withdrawn from the old exoskeleton, unless the leg were first injured outside of the joint.

Our analysis leads to the conclusion that we can neither account for the phenomenon of autotomy as due to internal causes alone in the sense of its being a general property of protoplasm, nor to an external cause, in the sense of a reaction to injury or loss from accident.   There would seem then only one possibility left, namely, that it is a result of both together, or in other words, a process that the animal has acquired in connection with the conditions  under which it lives, or in other words, an adaptive response of the organism to its conditions of life.

We are not, however, able at present to push these questions farther, for, however probable it may seem that animals and plants may acquire characteristics useful to them in their special conditions of life, and yet not of sufficient importance to be decisive in a life and death struggle, still we cannot, at present, state how this could have taken place in the course of evolution.   For, however plausible it may appear that the useful structure has been built up through an interaction between the organism and its environment, we cannot afford to leave out of sight another possibility, viz. that the structure or action may have appeared independently of the environment, but after it appeared the organism adopted a new environment to which its new characters made it better suited.   If the latter alternative is true, we should look in vain if we tried to find out how the interaction of the environment brought about the adaptation.   The relation would not be a causal one, in a physical sense, but the outcome of a different sort of a relation, viz. the restriction of the organism to the environment in which it can remain in existence and leave descendants.

# CHAPTER IX

## GRAFTING AND REGENERATION

By uniting parts of the same or different animals, or of plants, there is given an opportunity of studying a number of important problems connected with the regeneration of the grafted parts. Trembley's experiments in grafting pieces of hydra are amongst the earliest recorded cases of uniting portions of different animals, although in plants the process of grafting has been long known.[1] Trembley found that if a hydra is cut in two, the pieces can be reunited by their cut-surfaces, and a complete animal results. No regeneration takes place where the union has been made. He also succeeded in uniting the anterior half of one individual with the posterior half of another individual, and again produced a single individual. He failed to obtain a permanent union between different species.

More recently, Wetzel has carried out a number of different experiments in uniting pieces of hydra. He found that if two hydras are cut in two, the two anterior pieces may be united by the aboral cut-surfaces (Fig. 46, $B$), and the two posterior pieces may also be united by their oral cut-surfaces (Fig. 46, $A$). The fusion of these "like-ends" takes place as readily as when unlike ends are brought in contact, as in Trembley's experiments. Subsequently, however, regenerative changes take place. When, for instance, two anterior pieces are united by their aboral ends, there develop after two or three days one or two outgrowths, at or near the line of union, that become new feet, and the two individuals may subsequently separate. When two posterior pieces are united by their oral surfaces, a double circle of tentacles generally develops, one on each side of the line of union. The pieces then pinch apart and produce two hydras.[2] In another experiment the head and a part of the foot were cut from a hydra, and the head was turned around and grafted by its aboral surface upon the aboral surface of the middle piece. Another animal was cut in two in the middle, and the posterior half was grafted by its oral end to the oral end of the middle piece. In

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[1] For references to the literature on grafting in plants see Vöchting ('84).

[2] In one case they separated only after three months.

this way a new, artificial individual was made, as shown in Fig. 46, *C*, with the middle part of the body in a reverse direction as compared with the orientation of the two end-pieces.[1] The union of the three pieces was so perfect that not even a swelling or a constriction indicated the places of fusion. After six days a normal bud appeared at the region of union of the posterior and middle pieces, that gave rise to a new hydra, which separated after a few days. The com-
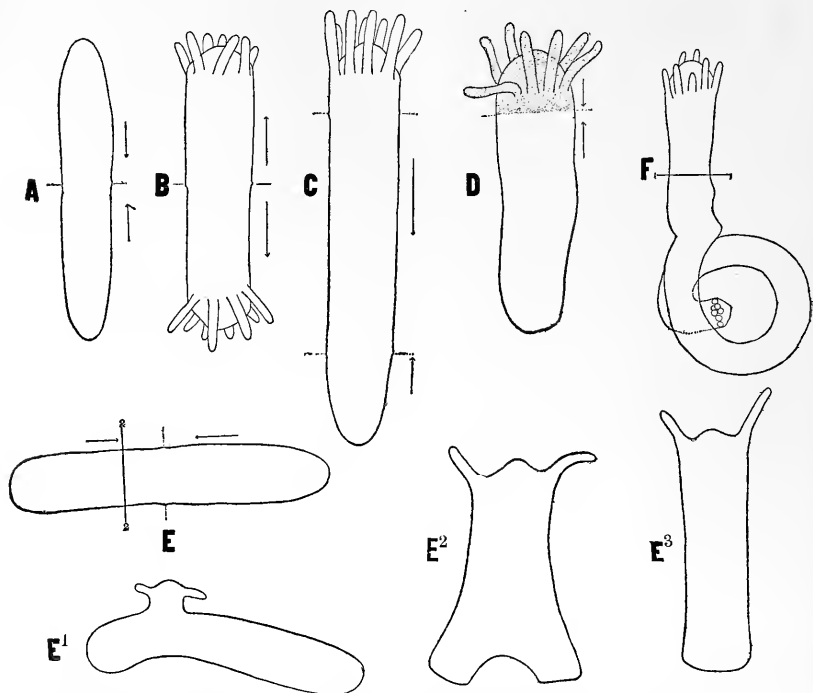


FIG. 46. — *A*. Two posterior pieces of hydra united by their oral ends. *B*. Two anterior pieces of hydra united by their aboral ends. *C*. A " long hydra " made by uniting three pieces; the middle piece reversed. *D*. After Peebles. Two posterior pieces of brown hydra united by oral ends, and one cut off near union. A new anterior end developed from the cut, aboral surface. *F*. After Peebles. Union of a nutritive and a protective polyps of hydractinia. Subsequently former cut off at line, 1–1. *E*. Union of two posterior pieces of hydra by oral ends. Subsequently one piece cut off at line, 2–2. *E*[1]. New head regenerated in region of union, and a foot from aboral cut-end. *E*[2], *E*[3]. Fusion of two parts with a single hydra.

pound animal was healthy and ate many daphnias. It was kept under observation for twenty-four days, and appeared normal, giving off several more buds.

In other experiments of this same sort a foot generally developed where the two aboral surfaces came together, and the head-end separated from the rest of the piece. In another case a mouth and tentacles appeared at the place at which the oral ends had united.

[1] This and other experiments were carried out by pushing the pieces on a bristle.

In a different kind of experiment, the anterior ends of two hydras were cut off and united by their aboral surfaces; then one of the components was cut in two, just back of the circle of tentacles. After five days two short, hook-like processes appeared at the cut, oral end. They produced a foot, by means of which the animal fixed itself. In this case it will be seen that a foot developed from an oral end. The result might not in itself be considered sufficient to show whether the development of a foot at the oral end of a piece is due to the influence of the other component, or is simply a case of heteromorphosis having no connection with the presence of the other component. Since heteromorphosis has never been observed in isolated pieces of hydra, the probability is that the result is in some way connected with the presence of the other component. Peebles has made a number of experiments, in which special attention was paid to this point. Fifteen anterior pieces were united in pairs by their aboral cut-surfaces, and then one component was cut in half, leaving an exposed oral end. Out of this number five pieces formed a new head at the cut-surface, and the pieces became attached by a foot, that developed at the region of union. Two others did not regenerate at the cut-surface, but became fixed as before, and neither regenerated nor became fixed at the cut-end. Three became attached at the cut, oral surface, but none of these developed a characteristic foot. The result shows, nevertheless, that some influence was present that inhibited the development of a mouth and tentacles at the oral cut-end, since these always develop in isolated pieces. In another series of experiments posterior ends were united by their oral surfaces, and then one of the two pieces was cut in two (Fig. 46, $E$). A new hypostome and tentacles developed at the region of union, and a foot at the aboral cut-surface, as shown in Fig. 46, $E^1$. An organism, with one mouth and a circle of tentacles, and two bodies and two feet, resulted. The bodies soon began to fuse together (Fig. 46, $E^2$) into a single one, and when the fusion had extended to the region of the feet, they also fused into a single structure (Fig. 46, $E^3$), so that a single hydra was produced.

In another experiment, twenty-two posterior ends were united in the same way, and then one of the two components was cut in two. In five cases a single head developed on the aboral end of the smaller piece (Fig. 46, $D$). It is evident in this case that the union of the two pieces has been a factor in bringing about the development of an aboral head. Another of the grafts produced an aboral head, and also one in the region of union. The remaining sixteen grafts produced new heads, if they developed at all, only in the region of union. Peebles states that the regeneration of aboral heads takes place only when one component is cut off near the region of union of the two pieces.

M

In general, it may be stated in regard to these experiments in hydra that when pieces are united in the same direction, that is, by unlike surfaces, a single individual is formed and no regeneration takes place where the union has been made, but when like surfaces are brought together, although perfect union may result, a process of regeneration takes place later, at or near the line of union. Even the presence of cut-surfaces at one or both cut-ends of the united components does not generally affect the result, although, in a few cases, it may change it, in so far that heteromorphic regeneration may take place from one piece. This sometimes leads to a suppression of regeneration at the line of union. The experiments do not show, perhaps, conclusively whether the heteromorphosis of the smaller component is due to the polarity of the larger component effecting a change in the smaller one, or whether the closing of the oral end of the smaller component (by its union with the other) brings about the result. All things considered, it seems to me that the larger component has directly influenced the other.

King has found that if two posterior pieces of hydra are united by the oral cut-surfaces, and then after they have fused *both pieces* are cut off *near* the line of fusion, there develops from the small piece *a single hydra*, with a foot at one end and tentacles at the other. If only one of the pieces is cut off *near* the line of fusion, a new head develops from its oral surface, as Peebles had found. If two anterior ends are united by their aboral cut-surfaces, and then later both are cut off near the line of fusion, a single hydra develops from the small, double piece. If one of the components is cut off near the line of union, a foot develops from the oral cut-end. If in any of the cases the cut is made some distance from the line of union, then each cut-surface develops its typical structure. These experiments leave no doubt as to the influence of the larger piece on the smaller one. Especially interesting is the formation of one individual from two short pieces united in opposite directions. In this case we must suppose that one piece has the stronger influence on the combination (perhaps because it is a little larger), and determines the polarization of the other piece.

King finds that when two posterior pieces are united by their oral ends, regeneration of one or of two heads often takes place at the line of union (Fig. 47, $B$, $B^1$, $B^2$), as Wetzel had found. If a dark green individual is united to a light green one, it can be seen that in many cases the new heads are formed by both components, as shown in Fig. 47, $B^1$. Later one of the posterior ends is absorbed, and the halves may then separate (Fig. 47, $B^1$, $B^2$). If a number of pieces are united, as indicated in Fig. 47, $E$, a number of heads may be formed, and one or more of these may have a double origin. No

evidences of separation of the pieces was observed in cases of this sort.

In one experiment two posterior pieces were united by oblique surfaces, as shown in Fig. 47, *C*, and one of the two was afterwards cut across, as indicated by the cross-line. The subsequent regeneration that took place is shown in Fig. 47, *C*¹. A head, com-
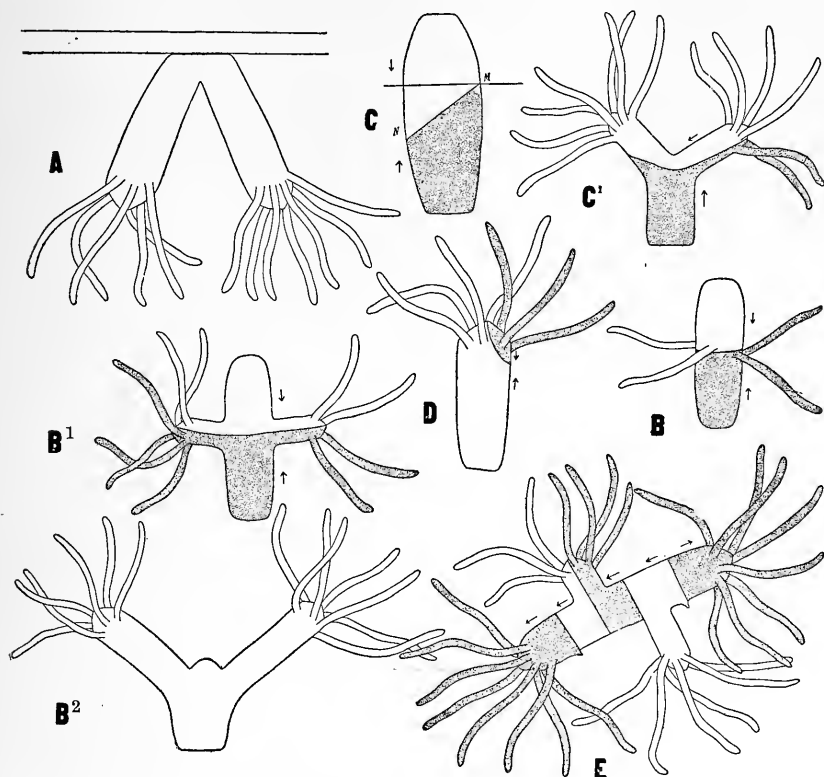


FIG. 47.—After King. *A.* Hydra split in two, hanging vertically downwards. Later the halves completely separated. *B.* Two posterior ends united by oral surfaces. *B*¹. Same; it regenerated two heads, each composed of parts of both pieces. *B*². Absorption of one piece leading to a later separation of halves. *C.* Two posterior ends united by oblique surfaces. Later one piece partially cut off, as indicated by line. *C*¹. Later still, two heads developed, one at *N*, the other at *M*. *D.* Similar experiment in which only one head developed, at *M*. *E.* Five pieces united as shown by arrows. Four heads regenerated, one being composed of parts of two pieces.

posed of parts of both pieces, developed at the cut-surface *M*, and another in the region *N* in Fig. 47, *C*, composed of material of one component. In another case, shown in Fig. 47, *D*, a head developed only at the cut-edge, but it was made up of material from both components.

A series of grafting experiments of another sort has been made

by Rand.   A part of one hydra is grafted upon the side of another
one in the following way.   A groove is scratched in a film of soft
paraffine covering the bottom of a dish filled with water.   Another
groove is made at right angles to the first one, and opening into it.
A hydra (the stock) is placed in the first groove, and a wound made
in its side with a knife.   Another hydra is cut in two, and one piece
(the graft) placed in the other groove, and its cut-surface brought
into contact with the wound in the side of the first individual.   If
the operation is successful the exposed surfaces of the two hydras
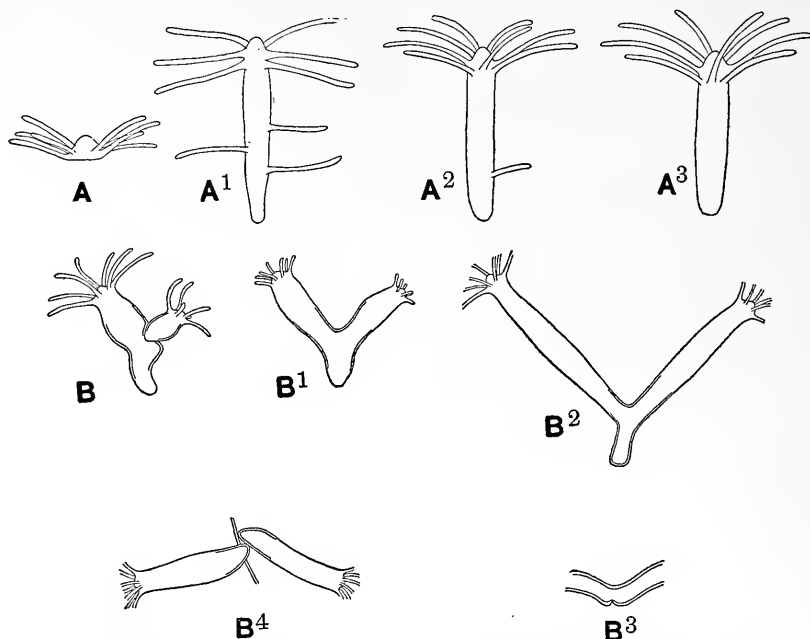


FIG. 48. — After Rand.   *A*. Head of Hydra cut off.   After eight days.   *A*[1]. Same after thirteen
days.   Three tentacles misplaced.   *A*[2]. Same after eighteen days.   *A*[3]. Same after twenty-
one days.   Misplaced tentacles absorbed.   *B*. Anterior end of *Hydra fusca*, grafted upon
side of body of another individual.   Half an hour after operation.   *B*[1]. Same after four days.
*B*[2]. Same after thirty-eight days.   *B*[3]. Same, foot-region after forty-nine days.   *B*[4]. Same
after separating.   Fifty-second day.

quickly unite, and the combination may be taken out of the groove.
If the piece grafted on the stock included about the anterior half
of a hydra, a two-headed animal results, as shown in Fig. 48, *B*.
Although the graft has been united to the side of the stock, it soon
assumes an apparently terminal position (Fig. 48, *B*[1]).   This is due
to the graft sharing with the anterior end of the stock the common
basal portion of the stock.   A slow process of separation of the two
anterior ends now begins, brought about by a deepening of the angle
between the halves (Fig. 48, *B*[2]).   This leads ultimately to a com-

plete separation of the two individuals (Fig. 48, $B^3$, $B^4$). Each may get a part of the original foot, or a new foot may arise on the graft as the division approaches the base.

In other experiments only a small part of the foot-end was cut from the animal that served as the graft. The long anterior piece was grafted as before upon the side of the stock. After the two had united, the graft was cut in two, leaving a part of the graft attached to the stock. The part regenerated tentacles, and in two cases subsequently separated from the stock as in the first experiment. In a third case the graft was absorbed by the stock as far as the circle of new tentacles, but its subsequent fate was not determined. In a fourth case the graft did not regenerate its tentacles, and was completely absorbed into the wall of the stock. The smaller the piece that is grafted on the stock the greater the chance that it will be absorbed, and furthermore short, broad rings are more likely to be absorbed than long, tubular pieces of the same volume.[1]

Rand's results show in general that when hydras are grafted together they regain the typical form in one of two ways, — either by separation into two individuals, or by the absorption of the smaller into the larger component. In the former case the result is brought about in the same way as when the anterior end is partially split in two and the halves subsequently separate. When the graft is absorbed it is not clear whether the absorbed piece disappears or, as seems not improbable, forms a part of the wall of the stock.

It is important to notice the difference between lateral buds and lateral grafts. The buds separate in the course of four or five days by constricting at the base, but this never happens in lateral grafts. Rand has also made some experiments with buds. He cut off the outer oral end of a bud, and grafted it back upon the stock in a new place. It did not separate from the stock as does a bud, but by a slow process of division it was set free in the same way as are lateral grafts. The proximal end of the bud, which was left attached, developed tentacles at its free end, constricted at its base, and was set free. The separation was, however, somewhat delayed.

In another experiment a bud was split in two lengthwise, and the cut was extended so that the body of the parent was separated into two pieces. Twenty-four hours later it was found that each half-bud had closed in, and was much larger than when first cut. The half-bud, that was attached to the posterior end of the anterior piece, was constricting at its base, and subsequently it separated at its point of

[1] Rand found that when a posterior piece was grafted by its cut, oral end to the side of another hydra that it was absorbed into the stock. In one case it moved down the whole length of the body of the stock and finally disappeared by absorption into the foot of the stock.

attachment. The other half of the bud, that had been left attached to the anterior end of the posterior piece, had swung around, so that its long axis corresponded to that of the posterior, parental piece. At first a slight constriction indicated the line of union of the two,



FIG. 49.—After Peebles. *A*. Grafting in *Tubularia mesenbryanthemum*. A small piece of the stock taken from the region near the base, and grafted in a reversed direction on the oral end of a long piece. *B*. Same with distal tentacles in small piece, and proximal tentacles in large piece (modified from Peebles). *C*. Same. Formation of hydranth (original). *D*. Like *A*. Both pieces produce hydranths. *E*. Protrusion of hydranths of last. *F*. Piece of oral end cut off, turned around and grafted on oral end of long piece. A single hydranth produced. Distal tentacle from both components. *G*. A short piece from distal (oral) end of long piece cut off, and grafted by its proximal end to proximal end of the same long piece.

but later this disappeared and a single hydra resulted. Whether the difference in the fate of the two half-buds is connected with their different polar relations to the parts of the parent, or is due to some other difference in the absorbing power of the anterior and posterior pieces, is not known.

Tubularia is not so well suited as hydra to show the influence of grafting on the united parts, since pieces of tubularia produce hydranths, both at the oral and aboral ends, although the latter hydranths take longer to develop. Peebles has shown, nevertheless, that grafting has an influence on the behavior of a piece. In order to show that the polarity of a small piece could be affected by a larger piece, the following experiment was carried out. After cutting off the old hydranth from the end of a stem, a short piece was then cut from the distal end of the same stem, turned around, and its oral end brought in contact with the oral end of the original piece, as indicated in Fig. 49, *F*. The two pieces, being held together for a few minutes, stuck together and subsequently united perfectly. From eighty-eight pieces united in this way the following results were obtained. Thirty-six formed a single hydranth at the end at which the grafting had been made. The distal row of tentacles appeared in the smaller reversed component, the proximal row in the larger piece (Fig. 49, *B*). The new hydranth pushed out later through the perisarc of the smaller piece (Fig. 49, *C*). In this experiment the smaller component was shorter than the average length of the hydranth-forming region. In two cases, in which the smaller component was larger, both circles of tentacles appeared in this piece. In six of the experiments the tips of the proximal tentacles arose from a part of the wall of the smaller piece, hence these tentacles had a double origin (Fig. 49, *F*). In five of the unions the smaller as well as the larger component produced a hydranth ; the two were stuck together by their oral ends (Fig. 49, *D*, *E*). The remaining four unions gave somewhat different results. In three of these the smaller piece produced only a part of a hydranth that remained sticking to the end of the hydranth formed by the larger component. In the thirty-six cases in which the minor component took part in the formation of the single hydranth, the influence of the larger component was shown not only in reversing the polarity of the smaller component, although this might in part be accounted for by the closing of the oral end of the smaller piece, but also in the time of development, since the hydranth appeared sooner than does the aboral hydranth and at the same time as does the oral hydranth.

In another series of experiments, a short piece was cut from the basal end of a long piece (three to four centimetres) and brought forward and grafted in a reversed position on the anterior end of the same long piece (Fig. 49, *A*). Of five unions of this sort, one produced a hydranth in each component, neither being reversed. Another of the pieces produced a hydranth partly out of each component (and at the same time another at the aboral end of the large piece). The other two pieces produced a single hydranth, a part of

which came from the minor component and appeared before the aboral hydranth on the aboral end of the larger piece. This last result shows that the small piece from the basal end has been affected by the oral end in such a way that it develops more rapidly than it would have done had it remained a part of the basal end.

In a third series of experiments a short piece (about a half of a millimetre) was cut from the anterior end of a long piece (one and five-tenths to two centimetres) and grafted *in a reversed position* on the posterior end of the same long piece (Fig. 49, *G*). In four cases a hydranth developed only at the oral end of the long piece and none from the aboral end or from the short piece. Eight unions produced, however, in the region of the graft, a hydranth formed partly by each component. Later another hydranth developed at the oral end of the larger piece. The latter results are not convincing, but they may show that the small piece has hastened the development of the hydranth at the aboral end.

Peebles has also made some experiments in grafting pieces of different members of the colonies of hydractinia and podocoryne. The colony of the former is made up of three different kinds of individuals : the nutritive, the reproductive, and the protective hydroids. A series of preliminary experiments showed that if these individuals are cut into a number of pieces each piece regenerates the same kind of individual as that of which it had been a part. It was also observed that if pieces of the nutritive individuals were allowed to remain quietly on the bottom of the dish they sent out branching stolons, which stuck to the bottom of the dish, and from these stolons there arose later nutritive hydranths that stood at right angles to the surface. When pieces of the same kind of individuals are grafted together, the results are essentially the same as with tubularia. If pieces of different kinds of individuals are united, the opportunity is given of testing the possible influence of one kind on the other. Peebles united a nutritive and a protective polyp by the cut, aboral ends (Fig. 46, *E*), and after they had grown together one of the polyps was cut off near the region of union, so that a small piece of a nutritive polyp was left attached to a protective polyp. When the piece of the nutritive polyp regenerated, it made a new nutritive polyp. The influence of the protective polyp was not apparent. If a nutritive and a reproductive polyp are united in the same way, and the latter cut in two near the line of union, a new reproductive polyp develops from the piece left attached to the nutritive polyp. Again there is shown no influence of the one on the other kind of polyp.

Hargitt has also made a number of grafting experiments on other hydroids. His most interesting results are those in which parts of two medusæ were united by holding their cut-surfaces together by

means of bristles passing through the individuals. Hargitt also finds that while in certain hydroids it is possible to bring about a union of oral with oral end, or aboral with aboral, or oral with aboral end of the same species,[1] yet a permanent union between different species cannot be brought about. These results are in agreement with those of a number of writers who have recorded the difficulty or impossibility of uniting parts of different species of hydra. In a few instances it has been possible to unite temporarily a piece of a brown hydra with a piece of a green one,— as I have also seen accomplished,— yet the pieces subsequently separate. Wetzel succeeded in obtaining better results with two species of brown hydras, *Hydra fusca* and *Hydra grisea*. In one experiment the head of *Hydra grisea* was grafted on the body (from which the head had been cut off) of *Hydra fusca*. After five hours the pieces seemed to have united. Later a constriction appeared at the place of union, and the head-piece produced a foot near the line of union, and the posterior piece produced a circle of tentacles at its anterior end. Eight days later, when the animal was being killed, it fell apart into two pieces. It was observed that during the period of union a stimulus to one piece was not carried over to the other. Wetzel's results seem to show that pieces of these two species of hydra unite at first, when brought together, as perfectly as do pieces of the same species, but the union never becomes permanent, a constriction appearing later at the line of union, and the pieces separating in this region. These results indicate, it seems to me, that the factors that bring about the first union are different from those that make the grafted pieces one organic whole. Other results indicate that the union of oral to oral end, or aboral to aboral end, while at first as perfect as between unlike surfaces, nevertheless is less permanent than when unlike surfaces are united; at least, subsequent regeneration is more likely to occur in the former than in the latter, and after this occurs the separation of the individuals often takes place. It seems, moreover, not improbable that a more permanent union results when similar regions are united by unlike surfaces, than when the union is at different levels. If, for instance, the anterior half of one hydra is united to the posterior half of another individual, the union is generally permanent; but if one or both of the pieces are longer than half the length, so that a "long animal" results, new tentacles are more often formed at the oral end of one component, and the parts subsequently separate. It may be that, at present, the data are insufficient to establish this general rule, and no doubt other modifying influences must be also taken into account; but it is important that attention should be drawn to this side of the subject.

[1] Pieces from male and female colonies of the same species also unite.

Grafting experiments in planarians have so far been carried out in only the two cases which I have described. In one of these the anterior ends of two short pieces of *Bipalium kewense* were united (Fig. 50, *A*). Neither piece produced a head at the region of union. Later the pieces were cut apart by an oblique cut that passed across the line of union (Fig. 50, *C*), so that each piece retained at its most anterior end (at one side) a piece of
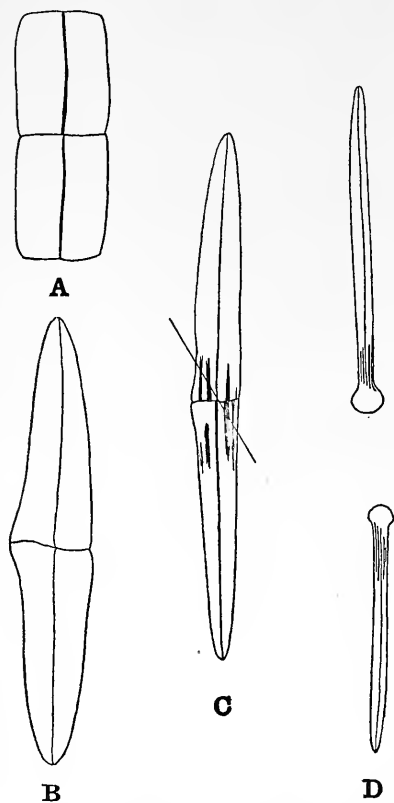


FIG. 51. — Two pieces of *Bipalium kewense* united by posterior ends. Each regenerated a head at anterior end.



A

B          D

FIG. 50. — *A*. Two pieces of *Bipalium kewense* united by anterior ends. *B*, *C*. Later stages of same. Line in *C* indicates how pieces were cut apart. *D*. Two worms produced by these pieces. All drawn to scale.

the other individual in a reversed position. A head developed at the anterior (and lateral) end of each piece, in such a way that a part at least of the small reversed piece was contained in the new head (Fig. 50, *D*). In the other case two pieces of bipalium were united by their posterior cut-surfaces. Each piece produced a new head at its free end, and the pieces greatly elongated, but remained sticking together (Fig. 51).

A large number of experiments have been made by Joest in grafting pieces of earthworms. The cut-surfaces were held in contact by means of two or three threads passing through the body wall of each piece and tied across, so that the pieces were drawn together and held firmly in that position. Joest found that pieces of the same or of different individuals could be united in various ways, and the union become permanent. If the anterior end of one worm is united to the posterior end of the same, or of another worm, a perfect union is

formed, and no subsequent regeneration takes place (Fig. 52, *A*). Long worms can be made by uniting two pieces, each more than half the length of a worm, or by uniting three pieces, as shown in Fig. 52, *C*. Short worms can be formed by cutting a middle piece from a worm, and uniting the anterior and posterior pieces (Fig. 53, *D*). Joest found that when a short worm is made in this way, so that no reproductive region is present, the new worm does not produce new reproductive organs. It is conceivable that new reproductive organs might
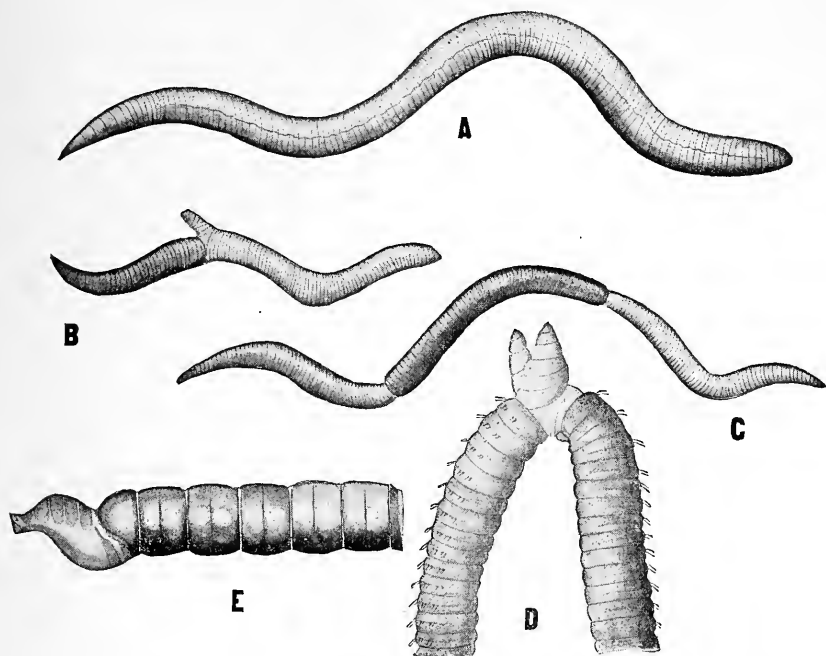


FIG. 52. — After Joest. *A*. Union of two pieces of *Allolobophora terrestris* in normal position. Twenty-two months after operation. *B*. Union of two pieces *Lumbricus rubellus*. Pieces turned 180° with respect to each other. *C*. Union of three pieces of *A. terrestris* to make a "long worm." *D*. Union of two worms (by anterior ends) from each of which eight anterior segments had been removed. After three months. Regenerating two new heads. *E*. A small piece of *Lumbricus rubellus* grafted upon *Allolobophora terrestris*. Former regenerated an anterior end.

have been produced either in the old segments, or by the formation of a new reproductive region between the two united pieces, but neither process takes place. In the long worms two sets of reproductive organs, etc., are present. This sort of union is, however, less permanent, as the worms often pull apart.

Joest also united two posterior ends by their anterior surfaces. In many cases no regeneration took place, and, in the absence of a head, the combination is destined to die, although it may remain alive, without food, for several months. When two very long pieces

were united by their anterior ends, — only eight segments being
removed from each worm, — although perfect union took place at
first, later one or two new heads generally developed at the region of
union (Fig. 52, *D*). When only one head developed it did not seem
to belong to one of the components rather than to the other, and
originated in the new tissue that appeared between the two pieces.
These experiments, in which the anterior surfaces of two pieces are
united, show also that the new head arises between the two pieces
most often, if not exclusively, when the union is in the anterior ends
of the worms. This corresponds with what is now known in regard
to the development of new heads by isolated pieces, since there is less
tendency to produce a head the farther posteriorly the cut has been
made. At more posterior levels a tail and not a head is often regen-
erated, as has been stated, on the anterior cut-surface. This forma-
tion of a heteromorphic tail seems to have been suppressed in the
pieces united in this region, except in one case,[1] in which it appears,
from Joest's account, that a tail probably regenerated, although Joest
speaks of it as a head.

It is more difficult to unite two anterior ends by their posterior
cut-surfaces, not because the surfaces refuse to unite, but because the
two pieces crawl away from each other and pull apart. In one case,
however, union of this sort was brought about.

In all the combinations that have been so far described, the
dorsal and ventral surfaces of both components were kept in the
same direction, so that the ventral nerve-cord of one piece came in
contact and fused with the nerve-cord in the other piece. Sometimes
it may happen that the components are not quite in the same position,
and the end of one nerve-cord may fail to abut against the other one.
In such cases Joest thinks that regeneration is more apt to take place
in the region of union, and he has carried out a series of experiments
in which the pieces were intentionally united, so that they are not in
corresponding positions. It is found that if one piece is turned so
that the nervous system lies 90 degrees, or even 180 degrees (Fig. 52,
*B*), from that of the other piece, the union takes place just as when
the pieces have the same orientation, except that the ends of the
nerve-cords do not unite. Subsequent regeneration from one or from
both components generally takes place in the region of union.

It is more difficult to unite pieces of different species of worms,
yet Joest has succeeded also in making combinations of this sort.
One union between the anterior end of *Lumbricus rubellus* and the
posterior end of *Allolobophora terrestris* was permanent, and the new
worm reacted as a single individual, and lived for eight months.
Each piece retained its specific characters, and showed no influence

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[1] See Joest's Fig. 14.

of the other component. By means of a similar experiment we have a way of finding out if one component can influence regeneration taking place from the other piece. Although Joest made only a few observations of this sort, the results show that no such influence is manifested.

By means of grafting it is possible to keep alive small pieces of a worm that would otherwise perish. For instance, pieces of a worm
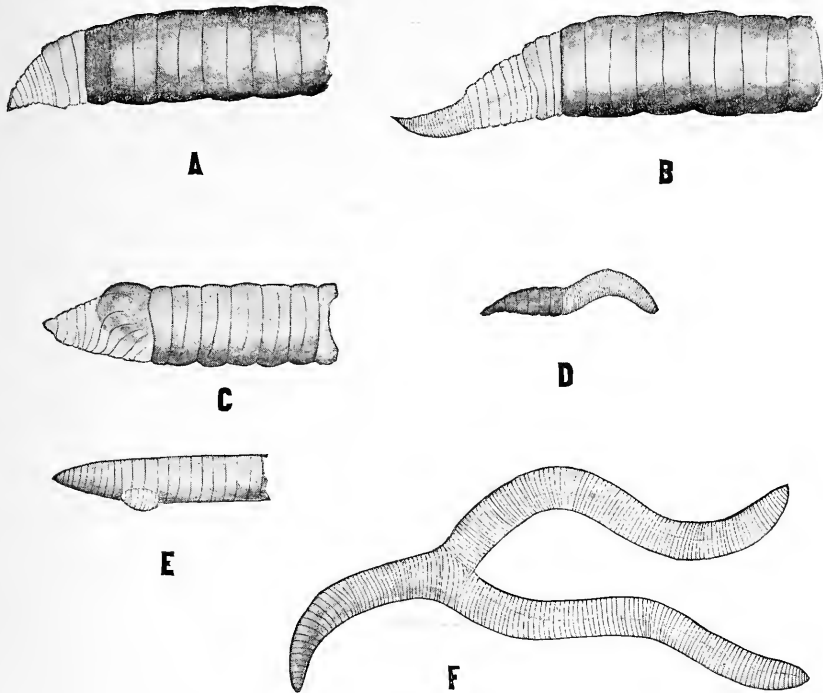


FIG. 53. — After Joest. *A.* Small piece of *Allolobophora terrestris* from posterior end grafted upon anterior end of another individual. Oral end free. Four weeks after grafting eight new segments formed. *B.* Same fourteen days later. A new part of thirty-seven segments had appeared at end of former eight segments. *C.* A piece of the body wall of *Allolobophora terrestris* grafted upon the cut-end (anterior) of *Lumbricus rubellus.* Two months later, as shown in figure, a head had grown on major component. *D.* Anterior and posterior ends of *A. terrestris* united to make a "short worm." *E.* A piece of body wall of *A. cyanea* grafted on side of body of *Lumbricus rubellus. F.* Piece of *L. rubellus* grafted on side of body of another individual to produce a double-tailed worm.

containing only three segments are not capable of independent existence, except for a short time, and even pieces of from four to eight segments die in most cases. It is not possible to unite small pieces of this size directly upon larger pieces, since they will die, ordinarily, as a result of the operation, but larger pieces can be united and then after union has been effected, one of them may be cut off near the place of union. The same result is sometimes brought

about accidentally by the worms themselves pulling apart and leaving a small piece of one component attached to the other.    Joest found that in several cases these small, attached pieces regenerated. In one case, after two long pieces had pulled apart, a small piece, left by one of the two, regenerated a single new segment with a mouth at its end.    In another case, after one of the components had been cut off, leaving two segments attached, a new part of seven segments regenerated.[1]    Especially interesting is the case in which two individuals (*A. terrestris*) had been united to form a long worm.    The anterior component extended to within two centimetres of the anus; the posterior piece had had the first four segments removed.    Three days later the anterior piece was cut off three segments in front of the region of union.    About a month later a small part of eight segments had regenerated from the cut-end (Fig. 53, *A*).    Fifteen days later another new part of thirty-seven segments developed at the end of the first new part (Fig. 53, *B*).    Joest speaks of the first eight segments as a head, and the second simply as a regenerative product. There can be little doubt, I think, that both parts represent a heteromorphic tail.    The region from which the regeneration took place would make this interpretation highly probable, and Joest's figures also indicate that the structure is a tail.    The result is very interesting, if my interpretation is correct, as it shows that the major component did not influence the kind of regeneration, although the surface of regeneration was separated by only three tail-segments from the anterior end of the major component.

In another experiment a long animal was made by uniting *Lumbricus rubellus* (whose posterior third had been cut off) and *Allolobophora terrestris* (whose first six segments had been cut off).    Four days later the two components had torn apart, but a small piece of the anterior worm remained attached to the anterior end of the posterior component.    The small piece consisted of the dorsal part of two and a half segments without any ventral part, so that the anterior end of the posterior component was partially exposed.    The small piece of lumbricus was much lighter in color, and this difference made it easy to distinguish between the two.    In less than a month the small transplanted piece had replaced its missing ventral part, so that the entire anterior surface of the larger component was covered over.    The small piece, in addition to regenerating its ventral part of four segments, had also begun to make new segments.    After a month and a half six new segments were present (Fig. 52, *E*), with a mouth at the anterior end.[2]    Even after ten months the color of

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[1] It is not certain whether this is a head or a tail.

[2] Joest states that this new part is a head, as shown by the presence of food matter in the digestive tract of the posterior piece.

the small piece was strikingly different from that of the major com-
ponent. The new head had the typical red-brown color of *L. rubellus*,
that forms a strong contrast to the grayish blue color of *A. terrestris*.[1]
The result shows that the color of the regenerated part has not been
influenced by that of the posterior component, and this is all the more
interesting, as Joest points out, because the small piece that was left
after the worms pulled apart was too small to have lived independently
for any length of time, and must have derived all its nourishment
from the larger piece.

In other experiments pieces of one species were cut from the side
of the body and grafted upon the cut-surface of the anterior end (or
elsewhere) of another species. In one of these experiments a piece
from the side of *A. terrestris*, that extended over five or six segments,
was sewed upon the anterior cut-surface of *L. rubellus* (from which
the anterior five segments had been removed). In about a month new
tissue appeared on the ventral side between the two pieces, and a
little later a complete head developed, whose dorsal side was made up
of the small piece (Fig. 53, *C*). The grafted piece was dark, and the
new, regenerated part light in color and continuous with the brown
color of *L. rubellus*, from which the new part had arisen. It is
important to notice that the four segments of the graft are completed
by four segments of the new part. After three months the new part
had assumed the red-brown color of *L. rubellus*. The color of the
grafted piece had not changed. We see in this case that even the
presence of a part of another worm in a regenerating region does not
have any influence, at least so far as color is concerned, on the new
part, even though its segments supplement some of those of the
new part. The new tissue seems to have come entirely from the
major component, and to have carried over the color characteristics
of the old part.

It has been shown that when two posterior pieces are united by
their anterior ends the combination must sooner or later die, since it
has no way of procuring food. The question arises : What will hap-
pen if one of the two components is cut in two near the place of
union ? Will a head then develop on the exposed aboral surface,
*because* a head is needed to adapt the worm to its surroundings, or
possibly, if it occurred, because the major component exerts some
sort of influence on the short, attached piece, as happens in hydra
and in tubularia ? Both Joest and I carried out an experiment
of this sort, and found that a tail and not a head regenerated, as
shown in Fig. 16, *F*. The experiment is, however, insufficient to
answer the question, since the region in which the second cut was
made is a region from which only a tail (and not a head) arises, even

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[1] The prostomium was misshapen, so that its specific character could not be made out.

when the oral end of a piece is exposed. In order to avoid this diffi-
culty I carried out another experiment. Two worms had the first
five or six segments cut off and the exposed anterior ends of the
worms united, as shown in Fig. 16, *D*. Then one of the components
was cut off, leaving three or four segments attached to the anterior end
of the other component. Although regeneration began in one case, it
did not go far enough to show what sort of a structure had developed,
but Hazen, who took up the same experiment, succeeded in one case
in obtaining a definite result. At the exposed aboral end of the
small piece a head and not a tail developed (Fig. 16, *E*). At first
sight it may appear that the result shows the influence of the major
component on the small piece, causing it to produce a head and not a
tail at its aboral end, but I think that this conclusion would be
erroneous, because it seems much more probable that we have here a
case of heteromorphosis, similar to that in *Planaria lugubris*, and that
the result depends entirely on the action of the smaller component.
It is hardly possible to demonstrate that this is the correct interpre-
tation, since if a small piece of this size is isolated it dies before it
regenerates. The result is paralleled, however, by the regeneration
of a tail at the anterior surface of a posterior piece.

The process of grafting has long been practised with plants, but
the experiments were made more for practical purposes than to study
the theoretical problems involved. Vöchting has, however, carried out
a large number of well-planned experiments. He finds that a stem
can be grafted upon a root, and a root upon a stem, a leaf upon
a stem or upon a root. Even an entire plant can be grafted upon
another. The results show, however, in general, that, whatever the
new position may be, the graft retains its morphological characters —
a shoot remains a shoot, a root is always a root, and a leaf a leaf.
Vöchting concludes that there is in the plant no principle or organi-
zation that conditions an unchangeable arrangement of the main
organs. "The inherited order of the parts, acquired apparently on
physiological grounds, may be altered by the experimentator; it is
possible for him to change the position of the building blocks within a
wide range without endangering the life of the whole." "It is essen-
tial, however, for the success of the experiment that the grafted
parts, or tissues, retain their normal orientation. If this condition is
not fulfilled there may take place, it is true, a union of the parts, but
sooner or later disturbances set in." Vöchting transplanted pieces in
abnormal positions, sometimes reversing the long axis of the grafted
piece, sometimes the radial axes, and sometimes both together. In
some cases this led to the formation of swellings that interfered with
the nourishment but carried with it no further consequences. In
other cases the changes went so far that the vital processes were inter-

fered with. At times an incomplete union took place between the parts; at others, even though the first union was perfect, death later ensued.

On the other hand, when similar pieces were grafted with their original orientation, a perfect union took place and the piece became a part of the stock. The results establish, Vöchting claims, that every part and every portion of a part has a polar orientation in one direction, and furthermore, in a body having a radially symmetrical form, there is also a radial polarization; that is, the inner side of each part is different from the outer side of the same surface, even though no such difference is apparent to us. The properties of the tissue-complex rest, in the last analysis, on that of the cells; the properties of the whole being only the sum total of the properties of its elements, so that we may say that every living cell of the root is polarized, not only longitudinally, but also radially; each has a different apical and root pole, a different anterior and posterior pole, and also right and left polar relations. These results, deduced from the experiments in grafting, lead Vöchting to formulate the following rule : " Like poles repel, unlike poles attract." This rule is the same as the law of the magnet. In fact, Vöchting states that the root and the stem relations show a remarkable resemblance, despite many differences, to a magnet. If the magnet is broken into pieces it may be reunited by bringing unlike poles together, but not by uniting like poles; the same statement holds for the root and the stem.

Exception may be taken, I believe, to parts of Vöchting's conclusions, especially in the light of the recent experiments in grafting in animals. It is by no means to be granted without further demonstration that the properties of the whole organism are only the sum-total of the action of the individual cells. If, as seems to be the case, the cells are organically united into a whole, the properties of this whole may be very different from the sum of the properties of the individual cells, just as the properties of sugar are entirely different from the sum of the properties of carbon, hydrogen, and oxygen.

The statement that like poles repel and unlike poles attract is, I believe, a conclusion that goes beyond the evidence. The experiments show that like poles do often unite in plants, and this has been abundantly shown to be the case in the lower animals, and even in forms as high as the earthworm and the tadpole. Even if when like poles are united subsequent changes take place, that in some cases, although apparently not in animals, lead to the death of the graft, it by no means follows that this has anything to do with the attraction or repulsion of the parts, but rather with some difficulty in obtaining food, or with the transportation of substances through the plant. In the lower animals we have seen that when like poles are united

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there is sometimes a stronger tendency to produce new organs at or near the place of union than when unlike poles are united, but it would be going too far, I think, to state that this is due to repulsion of the parts, especially in the sense in which the like poles of a magnet repel each other. It seems to be due rather to the two parts failing to unite into a whole organization, each retaining the same structural basis that it had before grafting, but this is a very different principle from that of an attraction and repulsion of the parts, and the question of the union of the parts appears also to be a different question from that of the organization of the parts themselves.

In the mammals, and in general in all forms in which there is a dependence of the parts on each other, it is impossible to carry out grafting-experiments on the same scale as those described in the preceding pages. The principal difficulties are to make the parts unite, and to supply nourishment and oxygen to the graft. Owing to the dependence of the parts of the body on each other for a constant supply of oxygen and food derived from the blood, as well as for the removal of the waste products, the parts cannot remain alive, or even in good condition, while new connections are being established. For this reason, as well as for others, it would not be possible, for instance, to graft the arm of a man upon another man. The tissue may have the power of uniting even in this case, as is seen when the bone is broken and subsequently reunited, but the difficulty would be in supplying the grafted arm with nourishment, etc., during the long time required for the union to take place. Smaller parts of the body may be successfully grafted, and there are several recorded cases in which parts of a finger, or of the nose, are said to have been cut off and to have reunited after being quickly put back in place. Pieces of human skin may be grafted without great difficulty upon an exposed surface, and it has been said that small pieces succeed better than larger ones, owing, most probably, to their being able to absorb sufficient oxygen, etc., and keep alive until new blood vessels have grown into the grafted piece.

There are a number of old and curious observations in regard to cases of grafting in higher animals. It was found by Hunter and by Duhamel that the spur of a young cock could be grafted upon the comb, when it continued to grow to its normal size. The comb, being richly supplied with blood, furnished the nourishment for the growth of the spur. Fischer transplanted the leg of an embryo bird to the comb of a cock, or of a hen, where it grew at first, but after some months degenerated. Zahn transplanted the fœtal femur to the kidney, where it grew for a time, but later degenerated. Bert transplanted the tail of a white rat to the body of *Mus decumanus*, where it continued alive ; but he found that the tail of the field mouse, *Mus sylvaticus*, did not grow so well on the rat, and the tail of a rat would not unite

at all with the body of a dog or of a cat. Bert bent over the tip of the tail of a rat, and grafted the distal end into the skin of the back of the same animal. After the tip had established union with the surrounding tissues, the tail was cut off at its base. The grafted tail remained alive, but did not regenerate at its free end.

There are several cases described by pathologists in which the skin of one mammal has been transplanted to another. The transplantation of the skin of the negro upon a white man has been brought about, but the evidence as to what subsequently happened is contradictory. It appears that while in many instances the transplanted skin has remained alive for a time, yet later it was thrown off by new skin growing under it and replacing it.

Leo Loeb has described a curious instance of grafting pieces of skin of different colors in the guinea pig. If a piece of black skin from the ear of a guinea pig is grafted upon the white ear of another animal, it unites and continues to live, but if a piece of white skin is grafted upon a black ear, it is slowly thrown off and replaced by new black skin that has regenerated around the edge of the graft from the tissue of the black ear.

In the literature of pathology there are many cases described in which parts of the body of mammals, particularly internal organs, have been grafted in unusual regions. The results have not always been the same, for while in some cases it appears that the operation has succeeded, in others the grafted part is subsequently absorbed, and in still other cases the graft may be at first partly absorbed and later begin to grow again. It appears that the establishment of an adequate blood supply is the most important element of success. Ribbert, who has made an extensive and successful series of experiments, has stated that the grafting takes place better when small pieces of an organ are used, since these can draw immediately on the surrounding regions for their oxygen, etc., while larger pieces are found to break down in the interior, owing to the fact that this part is too far removed from the supply of oxygen, food, etc. After the grafted piece has established a blood supply of its own, it may continue to grow. Ribbert transplanted small pieces of different tissues of the rabbit and guinea pig in, and upon the surface of, the lymph glands of the same or of another individual. The lymph gland was chosen because small pieces of tissue can be afterwards easily detected. A small piece of tissue about as large as a pin's head is cut off from whatever tissue is to be grafted, and as quickly as possible placed in a small cleft made in the lymph gland. After several days, weeks, or months, the gland is removed and the graft examined by means of serial sections.

Most of the experiments were made with "epithelial organs," and

according to Ribbert, if pieces of such organs are composed of epithelium only, they cannot be successfully grafted. For instance, the cells of the cornea can be readily separated from their underlying connective tissue, and can be kept alive in the lymph gland, but the cells diminish in number, show retrogressive metamorphosis in the direction of atrophy, and are finally absorbed. It seems that epithelium by itself cannot extract nourishment from its surroundings. Nothing is easier, however, than to transplant epithelium, if its connective tissue is present. The connective tissue furnishes so good a basis for nourishment that the epithelium not only lives, but may continue to proliferate. Ribbert finds that pieces of skin roll in after their removal. Then a process of growth takes place corresponding to that which follows a wound in the skin. The surface is closed and a small cyst is formed with a central cavity. The epithelium undergoes no changes during the first days or weeks. It remains stratified and shows an active process of cornification and desquamation. Similar results were obtained when pieces of the conjunctiva were transplanted, either under the skin in the anterior chamber of the eye, or in the lymph gland.

A small piece of the lining epithelium of the trachea with its underlying cartilage was also placed in the lymph gland. The epithelium grew, and covered over the wounded surface, forming over it only a single layer of cells. The old many-layered epithelium also became arranged in a single layer.

The wax glands, found in the inguinal folds of the rabbit, were also transplanted. The gland is composed of closed, compressed alveoli, surrounded by large, polygonal, clear cells. Small pieces of a gland, transplanted upon the lymph gland, underwent characteristic changes. The cells of the alveoli were changed into a stratified epithelium; and broken-down cells, and wax, were found in the interior of the alveoli. The central alveoli underwent the greatest change, while some of the peripheral alveoli that were in contact with the lymph gland remained unchanged. It seems that the difference is due to the better nourishment of the outer alveoli. After several months the alveoli swell up and degenerate. Transplanted pieces of the salivary glands also change, the alveoli producing a lining epithelium like that of the transplanted wax gland. The same change was observed in a piece of a salivary gland transplanted in the body cavity.

Small pieces of the liver were cut off and placed in the lymph gland. They did not always grow as well as did the preceding tissues, but often went to pieces. If they healed, the liver tissue often remained unchanged for several weeks. After two or three weeks connective tissue appeared between the peripheral liver cells, separating the cells from each other. The cells grew smaller, their

protoplasm disappeared, and they at last disintegrated. Pieces of the gall duct behaved differently. They sometimes showed active growth, leading to the development of numerous branched canals.[1]

Pieces of the kidney, when transplanted, suffered a great change, and were subsequently absorbed. Transplanted pieces of a testis also changed. After six days, Sertoli's cells and the spermatozoa disappeared. A kind of indifferent cell remained, characterized by clear protoplasm and by a large nucleus. After seventeen days further changes were observed, and later the pieces were completely absorbed. Pieces of the ovary rapidly disappeared, leaving only a mass of interstitial connective tissue.

The connective tissue underwent, in all the transplanted pieces, characteristic changes. The tissue became less dense, the protoplasm and nucleus of each cell enlarged. The cells multiplied, but only very slowly. These changes took place after one or two days. After a month or two the cells became more compact, their processes more numerous, and the nucleus small and long. Later degeneration set in.

Small pieces of bone from the caudal vertebræ were also transplanted, care being taken that each piece should contain some of the periosteum and marrow. The bone tissue goes to pieces, but the periosteum and marrow develop further. New bone is formed from the cells of the marrow as well as from those of the periosteum. Finally the entire piece, both its old and its new parts, is absorbed. Pieces of muscles were also absorbed.

These experiments of Ribbert show that transplanted pieces of tissue do not increase in size by growth, but undergo changes which he describes as a return to an earlier condition of development. The abnormal condition of their existence seems to be the cause of this change. The transformation may be due to a change of nourishment, or to a loss of nerve influence, or to lessened functional activity.

These results have a direct bearing on the problem of regeneration. They show that all kinds of tissue may continue to live, and the cells multiply in different parts of the body, but there seems to be nothing in these cases comparable to a regeneration of the entire organ. In the new situation the cells often assume an entirely new arrangement. After a period of activity, a process of degeneration commences, and the piece atrophies. Ribbert thinks that the atrophy is due to lack of nourishment, yet it is not clear how this could be the case, since for the first few weeks after transplantation there is an active growth, and in some cases, as in that of the bone, there is a formation of new, characteristic tissue. It may be that the trans-

[1] It is known that the process of regeneration of the liver takes place especially from the gall ducts.

planted tissues can no longer manufacture the substances necessary for their specific growth, and after the materials that have been brought along with them have been used up, the growth of the piece is stopped and its subsequent degeneration begins.    It would be interesting to see if pieces transplanted to the same kind of organ as that to which they belong will become permanently incorporated in their new position.

The grafting-experiments that have been described in the preceding pages were carried out with pieces of adult organisms.    Somewhat different conditions are present when parts of the developing egg or embryo are united, inasmuch as a process has been started in them that may go on independently, to a certain extent, of the union of the pieces.    Born has carried out a large number of experiments in grafting parts of tadpoles of the same species, and also of different species.    The union is brought about at the time when the tadpoles are about to leave the jelly membranes.    The cut-surfaces are brought in contact and the pieces pushed together and held in place for an hour or two by means of small silver blocks or pieces of wire. The pieces readily stick together, and the union is a permanent one. Before describing Born's results, it may be well to consider the power of regeneration of young tadpoles.    If the tail is cut off a new one is regenerated by the tadpole, but all parts of the body do not have this same power.    Schaper found that if a part of the brain, or even the entire brain, is removed, no regeneration takes place.    I have found that if the region where the heart is about to develop is cut out from a young embryo, a new heart is not formed.[1]    If a tadpole is cut in two across the middle of the body, neither piece regenerates the missing half.    Byrnes has found, however, that if the region from which the posterior limb develops is cut out a new limb regenerates. In older tadpoles, Spallanzani found that if the hind limb is cut off it will regenerate, and Barfurth has more recently confirmed this result.    The end of the tail that has been cut off from a young tadpole, before the tail has begun to differentiate, may continue alive for several days.    It grows larger and flatter, and the V-shaped mesoblastic somites are formed.    A slight regeneration even starts at its anterior end, as first observed by Vulpian and later by Born.    The notochord and nerve-cord may send new tissue into the new part, and even some of the muscle cells may extend into this part, but the piece dies before regeneration goes any further.    If, however, the tail is grafted in a reverse direction on the body of another tadpole, the regeneration may go further and produce a *tail-like* structure, as Harrison discovered and as I have also seen.

[1] In one case I observed rhythmic pulsations in a vessel on one side of the neck, in the region above the pharynx.

Born found that if the anterior half of one tadpole was united to the posterior half of the same or of another tadpole a single individual was formed which he kept alive in several cases until the time of metamorphosis. If the head of a tadpole is cut off and grafted upon the side of the body of another tadpole, the head will remain alive and continue to develop in its new position, and, if well nourished by means of the connecting blood vessels that develop, it may grow to be as large as the head of the tadpole to which it is attached. Similarly, if the tail of one tadpole is grafted upon the side of the body of another tadpole, it also continues to develop, and at the time of metamorphosis, when the normal tail is absorbed, the additional or misplaced tail also shows signs of breaking down. Even the posterior half of one tadpole, if grafted to the ventral side of another, may continue to develop, producing legs, etc.

Born succeeded in uniting tadpoles of different species in several different ways. They were united by their heads or by their ventral surfaces, or longer and shorter tadpoles made by using pieces longer or shorter than a half. In all of these cases there is no regeneration at the place of union, and the internal organ, the digestive tract, nervous system, and blood vessels unite when brought into contact. When pieces are united end to end, like organs unite to like, the nerve-cord with the nerve-cord, digestive tract with digestive tract, segmental duct with segmental duct, cœlom with cœlom, and although less often, the notochords sometimes join together. The lack of union of the ends of the notochord is explained by its frequent partial displacement at the cut-end, for when the cut is made the notochord, being tougher than the other structures, is often dragged out of place in one or in both pieces, so that the ends do not meet when the pieces are put together. When like organs are brought together the substance of one unites directly with the substance of the other, and if the organ is a hollow one, as is the digestive tract or the nerve-cord, their cavities also become continuous. There is also, Born states, some evidence to show that if similar organs are not brought exactly in contact their ends find each other and unite, and if they do not at first meet squarely they may do so later. When the ends of unlike organs are brought in contact, as, for instance, the nerve-cord and notochord, they do not unite, but connective tissue develops between them. The union of like parts, Born suggests, may be due to some sort of cytotropism, the outcome of a mutual attraction between similar cells like that which Roux has observed between the isolated cells of the segmented egg of the frog. Born thinks that the first rapid union of the pieces is due to the attraction of the ectoderm of one component for that of the other.

Born succeeded also in uniting pieces of the tadpoles of different

species, even when they belonged to different genera. It is found, however, that some of these combinations can be more easily made than others, but it is not clear whether the difference depends upon differences in the sizes of the pieces, or the rate of growth of the ecto-
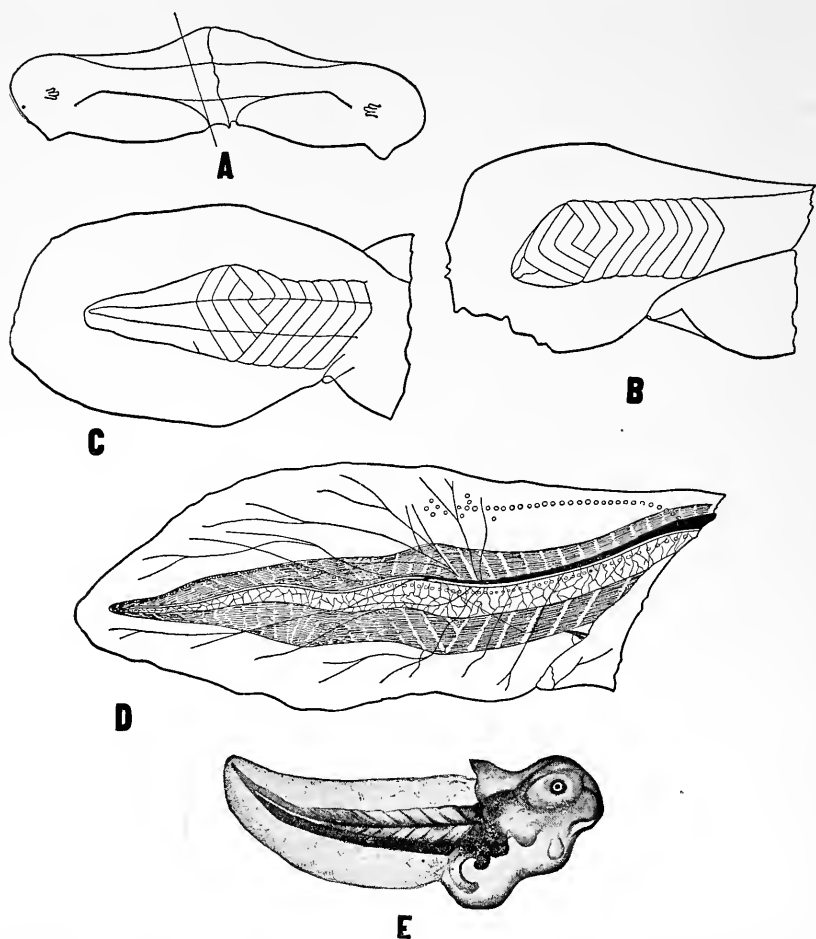


FIG. 54. — *A*. After Harrison. Union of two tadpoles by posterior ends. Two days after opera-tion. The line to the left of plane of union indicates where the two were cut apart. *B*. Tail of right-hand tadpole in *A*. Five days after cutting apart. *C*. Same. Nine days after cut-ting apart. *D*. Same. Ninety-five days after cutting apart. *E*. After Born. Combination of *Rana esculenta* (anterior) and *Rana arvalis* (posterior). Thirteen days after the operation.

derm over the cut-surfaces, or to a deeper-lying lack of affinity between the tissues. A combination of *Rana esculenta* (anterior) with *Bombi-nator igneus* (posterior) was made. The combination lived for ten days, and then showing pathological changes, it was killed. Another combination is shown in Fig. 54, *E*, in which the anterior part of *Rana*

*esculenta* was united to the posterior part of *Rana arvalis*.[1] The blood of the posterior component was driven through the vessels by the action of the heart of the anterior component. The animal lived for seventeen days.

In all these combinations between different species, each developing part retains its specific characters, and, although in several cases one part received its nourishment from the other through the common circulation, yet no influence of one component on the other could be observed.

Harrison has succeeded in keeping an individual made up of two species, *Rana virescens* and *Rana palustris*, for a much longer time,— until, in fact, the transformation of a tadpole into a frog had taken place. Each half retained the characteristic features of the species to which it belongs.

The absence of regeneration after the union of the pieces may be attributed, in several cases, to the absence of this power in the region through which the cut has been made ; but in other experiments this cannot be the explanation, since the power to regenerate can be shown to exist in the part. This is the case in an experiment carried out by Harrison and repeated later by myself. If the tips of the tail of two tadpoles are cut off and interchanged (Fig. 55, *A*, *B*), a perfect union takes place between the two parts, and a single tail develops. Each of the cut-surfaces has the power to regenerate, but the union of the parts has suppressed the regeneration. If, however, like parts are not brought in contact, regeneration may take place in the region of union (Fig. 55, *D*).

Both Harrison and I have made a number of experiments, in which the end of the tail of a tadpole of one species was interchanged with a similar part of another species. It is found that as the new tail grows larger the ectoderm of the grafted piece is carried out to the tip of the new tail, as shown in Fig. 55, *C*, and does not cover all the inner tissues that belong to the same piece, the rest of the tail being covered by the ectoderm of the major component. If the tip of the tail is now cut off, as indicated by the line *b–b* in Fig. 55, *C*, there are left at the exposed edge two kinds of ectoderm, and from the cut-edge a new tail regenerates, covered in part by each of the two kinds of ectoderm. I made this experiment in order to see if the new ectoderm would show any influence of its dual origin, especially along the line where the two kinds are in contact, but no influence could be detected. In another series of experiments the grafted tail was cut off, as shown in Fig. 55, *A*, or in Fig. 55, *B*, or in Fig. 55, *C*, *a–a*. In these cases there is left exposed, at the cut-edge, the internal tissues of the two species. The new tail

[1] The figure was drawn fifteen days after union.

that regenerates is composed in part of material derived from one species and in part from that of the other, but each tissue remains true to its kind, and there is found no evidence of an influence of one on the other (Fig. 55, *E*). These experiments show that even when the two kinds of tissue regenerate side by side, and unite to form a single morphological organ, there is no influence of a specific kind of one tissue on the other.
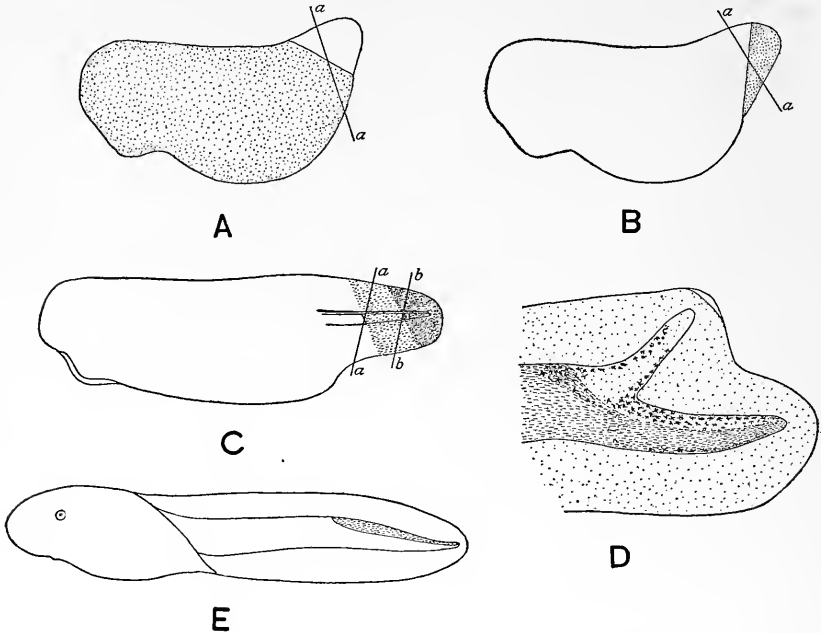


FIG. 55. — *A. Rana sylvatica* with grafted tail of *Rana palustris*. Line *a–a* indicates where tail was cut off. *B. Rana palustris* with grafted tail of *Rana sylvatica*. Line *a–a* indicates where tail was cut off. *C.* Older stage of a graft like *B*. Lines indicating two possible operations. *D.* Another individual with two tails, one composed of both components. *E.* Later stage of last, when tail was cut off at level *a–a*.

Another series of experiments in grafting, similar to one of those made by Joest and myself on the earthworm, has been made by Harrison on the tadpole. I have also later made similar experiments. Two tadpoles are united by their posterior ends, as shown in Fig. 54, *A*, and a day or two after union one of the tails is cut off near the line of union. There is thus left attached to the end of the tail of one tadpole a part of the tail of the other united in a reverse direction, so that the exposed cut-end is the anterior end of the small piece. There grows out from this cut-end a structure that resembles a tail (Fig. 54, *B*, *C*, *D*). It contains a continuation of the notochord and nerve-cord, that taper in a characteristic way to the end of the new structure. The tail is flat and has a central band of muscle tissue, and

a dorsal and ventral fin. The muscles of the normal tail have a characteristic V-shaped arrangement with the apex of the V's turned forward, but unfortunately in the new tail the muscles are so irregular that it is impossible to make out their arrangement (Fig. 54, *D*). If the new part is in reality a tail, the V's ought to stand in the same way as do those in the major component, and opposed to the V's on the part from which the new material arises. If the new structure is not a tail at all, but a new growth, or even a suppressed trunk, then the V's should stand as in the small part itself. It has not been possible as yet to obtain a decisive case. Harrison obtained one case in which the arrangement of the muscles in the new part seemed to be more as it should appear if the new part is a heteromorphic tail (Fig. 54, *D*). Even if this could be shown to be the case, it may be that under the conditions of the experiment the arrangement of the muscles is determined by the use of the tail, although this does not seem very probable. Harrison, after a careful analysis of the question, left it undecided, but seemed more inclined to the view that the result is due to the development of something new rather than a heteromorphic growth. On the contrary I am strongly inclined to believe that the latter is the true explanation. In another way I have been able to bring about the development of the same structure. A small triangular piece is cut from the upper part of the tail, as indicated in Fig. 56, *A*, one point of the triangle passing through the notochord, or even through the aorta. If the cut-surfaces are kept apart for a few hours, until the exposed end has been covered over by ectoderm, they may not unite afterward, and two exposed surfaces are left,—one at the distal end of the base of the tail, and the other at the proximal end of the outer part of the tail. The latter surface corresponds to that in the grafting-experiment. Regeneration may take place from the two surfaces; both new parts seem to be exactly alike, and both resemble a regenerated tail. The one from the proximal surface of the outer part of the tail contains a notochord, nerve-cord, connective tissue, pigment cells, and muscle tissue (Fig. 56, *B*). The arrangement of the muscle fibres is generally very irregular, and the characteristic V-shaped arrangement cannot be detected.

In only a few cases have attempts been made to unite two eggs or two very early embryos, although there are a few casual observations [1] in which such a fusion has been observed. The problems that arise in connection with the union of two eggs are full of interest. Each egg has the power of producing an embryo of normal size. If two eggs are united into one, will a single giant organism result, or two organisms? If the former, we must suppose that a new organization is formed of double size. Whether an upper limit of organiza-

[1] Metschnikoff ('86), Herbst ('92).

tion exists can only be determined by such an experiment.  If two
fused organisms result from the fusion of two eggs, it would show
the structure of the egg is of such a kind that two organizations can-
not readjust themselves into a single one of double size.   Moreover, it
is important to discover whether any difference exists as to the stage
of development at which the union is brought about, for it is conceiv-
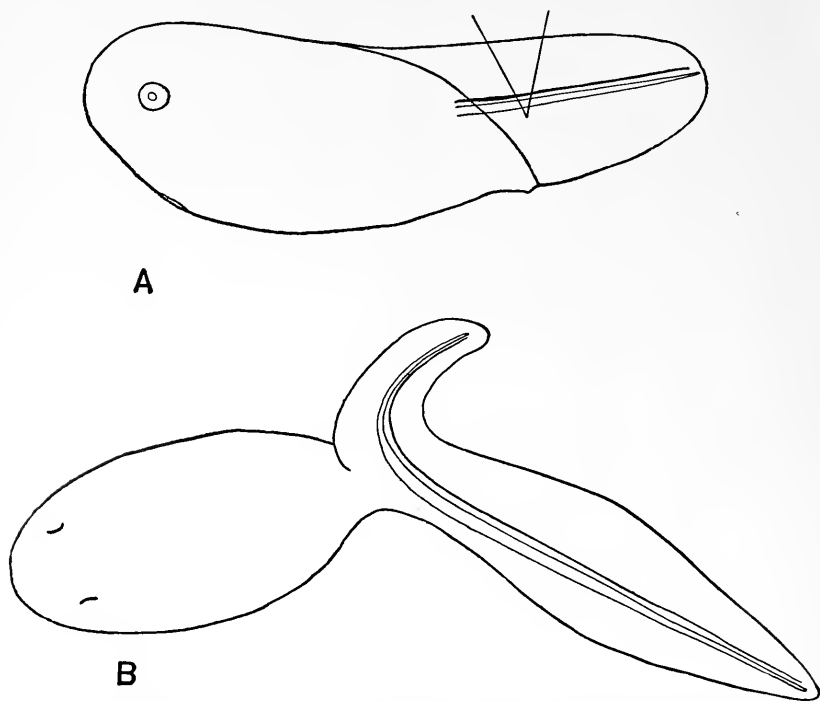able that while a rearrangement is possible at one stage, it might
not be at another.



FIG. 56. — *A*. Tadpole to show where the V-shaped piece is cut from the tail.  *B*. Later stage of
same with a new tail-like outgrowth from the anterior end of tail.

It has been shown that two blastulæ of the sea-urchin can be
united to form a single embryo.   I found ('95) that occasionally two
blastulæ stick together and fuse, so that a single sphere of double
size is formed.   As a rule two gastrulæ and two more or less com-
plete embryos develop from each double blastula, but in a few cases
I found that a single embryo may be formed, that shows, however,
traces of its double origin.   Driesch has more recently (1900) suc-
ceeded [1] in bringing about more readily a union of two segmenting

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[1] Eggs without membranes were placed in sea water without calcium, to which a few
drops of sodium hydroxide have been added.

eggs or blastulæ, and obtained perfect single individuals from two fused blastulæ. He finds that if the fusion takes place at an early stage the resulting embryo is less likely to show its double origin than when older blastula stages are united. Zur Strassen has also observed giant embryos of ascaris that arise by a fusion of two eggs. Loeb has found that the eggs of chætopterus, which can be made to develop parthenogenetically in certain salt solutions, often stick together and produce giant embryos.

# CHAPTER X

## THE ORIGIN OF NEW CELLS AND TISSUES

THERE are many difficulties in the way of determining the origin of the cells that make up the new part. The only means at present at our command for studying their source is by serial sections of a number of different stages taken at intervals from different animals. Since there may be differences between the processes in different individuals, and since we can only piece together the information gained from successive stages, much uncertainty exists in regard to the changes that take place during regeneration, even in some of those forms that have been examined over and over again. Were it possible actually to follow out the movements of the living cells in one and the same animal, the problem would offer fewer difficulties, but this cannot be done. It will be more profitable to consider first the better-known and simpler processes, and afterward those that are less well-known.

The regeneration of the head and tail of lumbriculus and of certain naids is a comparatively simple process, and has been studied by several investigators, whose results agree, at least in regard to the most essential features. Semper ('76) described the origin of the new organs in the formation of new individuals by budding in nais. He found that the new brain and nerve-cord develop from the ectoderm, the new mesoderm also from ectoderm, and the new digestive tract from the old one, except the pharynx, which arises by the fusion of two mesodermal "gill-slits." Bülow ('83) studied the regeneration of the tail of lumbriculus. He found the ventral cord in the new part arising from a paired ectodermal thickening, the mesoderm arising from a proliferation of cells. These cells are invaginated in the region between ectoderm and endoderm — the in-turning of the proctodæum being looked upon as an endodermal invagination.[1] The more recent work of Randolph, Rievel, Michel, Hasse, Hepke, and von Wagner on the same or related forms has served to point out certain errors in the earlier work of Semper and Bülow, and has added some new and important facts, especially in connection with the origin of the mesoderm in the new part. Without attempting to give a detailed account of these results,

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[1] The usual interpretation at present is to regard the proctodæal ingrowth as ectodermal.

I shall describe the principal changes that have been found to take place. When the anterior end of lumbriculus or of tubifex is cut off, the cut-surface very quickly closes, as a result of the contraction of the body wall. According to some investigators, the circular muscles are chiefly concerned in the closing, but according to others the longitudinal muscles bring about the result. The cut-end of the diges-
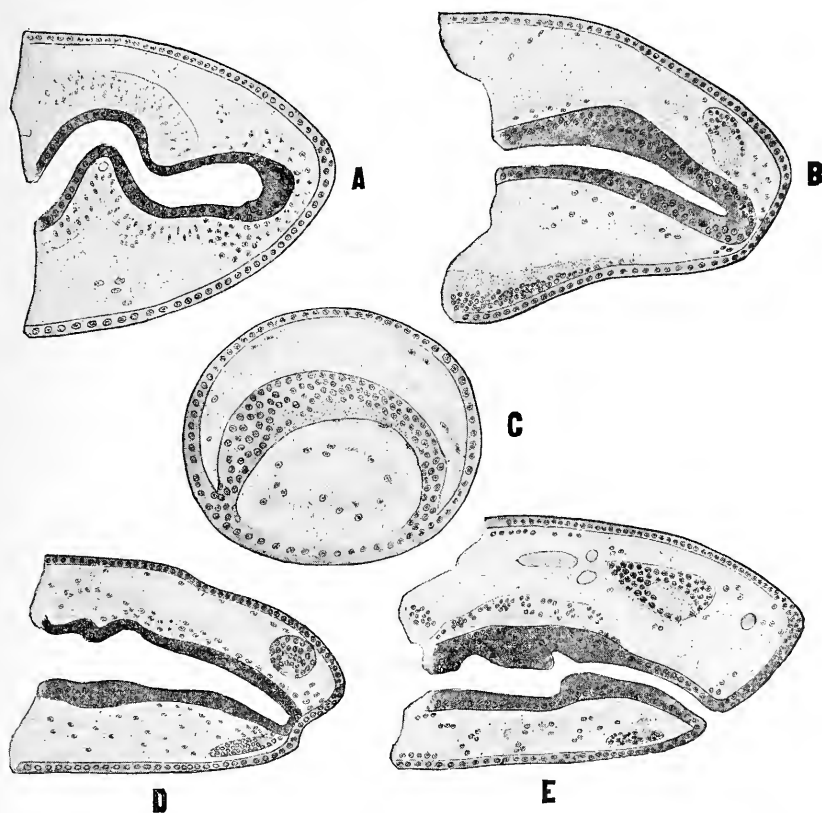


FIG. 57. — After Hasse. Regeneration of *head* of *Tubifex rivulorum*. *A*. Sagittal section of anterior end. Six days after cutting in two. *B*. Eleven days after cutting in two. *C*. Cross-section through new part. Five days after operation. *D*. Fourteen days after operation. *E*. Sixteen days after operation.

tive tract is pulled a little inward, and its end also closes (Fig. 57, *A*). For a day or two no important changes can be observed to take place, but new ectoderm soon appears over the cut-surface. This ectoderm arises in all cases from the old ectoderm, and as it increases in amount the old ectoderm is pushed back from over the cut-end, leaving a layer composed of a single row of cells over the end. Since nuclei in process of division are rarely present before these initial

processes begin, it is probable that the changes are due, in large part, to an out-wandering of ectodermal cells, or, what amounts to the same thing, to the leaving behind of cells as the old ectoderm withdraws from the cut-end.    In the new ectoderm over the end, an active process of proliferation takes place (Fig. 57, *B*), that leads to the production of a large number of cells lying within the new part.   The ectoderm has at this time begun to bulge outward, so that the proliferated cells come to lie within the dome-shaped beginning of the new head.    There appears to be some difference in the number and in the location of the proliferations in different species.    In general, the new cells arise from the ventral and ventro-anterior region of the dome-shaped ecto-dermal covering of the new part.    Most of this new material gives rise to the  brain, commissures, and  ventral  nerve-cord (Fig. 57, *C*). The cells giving rise to these structures in tubifex come from two ven-tral regions of proliferation that extend along the sides and dorsally to the anterior end in front of the digestive tract.    Where the two masses meet above and in front, the brain is formed.[1]   The cells that do not take part in the formation of the nervous system give rise to the mus-cles and connective tissue of the new head.   These cells lie especially at the outer sides of the proliferated mass.    The origin of the new muscles from ectoderm stands in sharp contrast to the current ideas in regard to the origin of new tissues, and yet it is a point on which the more recent investigators are entirely in accord.   Michel, Hepke, and von Wagner have arrived at the same conclusion after a careful examination, and there seems to be no reason for refusing to accept their results.    The theoretical importance of this discovery will be discussed later.

Soon  after  the  proliferation  from  the  ectoderm  has  begun,  the blind  end  of  the  digestive  tract  starts  to  push  forward (Fig. 57, *D*). The cells in the most anterior part of its wall begin to divide, and the end grows in an anterior direction as a more or less solid rod.   This rod extends, in some species, as far forward as the ectoderm, meeting the  latter  on  the  inner  side  of  its  antero-ventral  surface.    At this point an in-turning of ectodermal cells, in the form of a blind pit, develops, and later this pit, deepening to become a tube, forms the mouth cavity.   Its inner end is from the beginning in contact with the anterior end of the digestive tract, or else it connects with the latter soon after its formation.   The two flatten against each other, the cells draw away in the middle of the region of contact, and the cavity of the new mouth becomes continuous with the cavity of the old digestive tract.   The mouth lies at first nearly terminal in posi-tion (Fig. 57, *E*), but by the forward growth of the body wall over

[1] In some species the two proliferating regions seem to be in contact above from the beginning (Hepke, in *Nais*).

and in front of the mouth to form the prostomium, the mouth comes later to lie more on the ventral surface. The short tube produced by the in-turned ectoderm forms only a short part of the digestive tract. It leads from the mouth opening to the new pharynx, and forms, therefore, only the buccal cavity. A similar ectodermal tube, the stomodæum, which develops in the egg-embryo, becomes not only the buccal chamber, but also the lining of the pharynx. The latter is, therefore, considered an ectodermal structure in the embryo. On the other hand, in the regenerated head the lining of the new pharynx arises from the anterior part of the endodermal digestive tract. We find, therefore, that the same organ, the pharynx, may arise in the same animal from distinct "germ-layers." This result also has an important bearing on our ideas concerning the value and meaning of the so-called "germ-layers," and has helped to bring about a revolution of current opinion as to the importance of these layers.

The preceding account of the development of the head has shown that while certain of the new organs and layers arise from the same organs of the old part, yet this is not true for all of them. Thus while the ectoderm gives rise to ectoderm, the new muscles do not appear to come from the old ones, or even from other mesodermal tissues, but from the ectoderm. The old digestive tract gives rise to the greater part of the new one, but the new pharynx comes from the old endoderm, and not from the in-turned ectoderm. The nervous system does not arise from the old ventral cord, but from a proliferation of ectoderm. It has, thus, the same origin as the nervous system of the embryo. The origin of the new blood vessels has not been satisfactorily made out. The seta sacs arise from ectodermal pits as in the embryo.

In regard to the origin of the new mesoderm, the evidence is still insufficient, I think, to show that cells derived from the old muscles or peritoneum take no part in the formation of the new muscles and peritoneum; but that the greater part of the new muscles, etc., comes from the proliferated cells can scarcely be doubted. This latter discovery loses none of its significance, however, even if it should prove true that the old muscles, etc., contribute something to the new part. It is also not entirely disproven that the ventral nerve-cord does not take a small share in the development of the new cord.

The regeneration of a new tail-end in these same forms appears to take place in much the same way as the head. The cut-end quickly closes; later a layer of ectoderm appears over the posterior surface, and the new part bulges out and becomes dome-shaped. A paired, or in some species a single, region of proliferation develops from the ectoderm, that gives rise to the new ventral nerve-cord.

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Lateral proliferations of ectoderm produce, according to some writers, the material out of which the mesoderm of the new tail is formed. Randolph, on the other hand, has described the new mesoderm as arising from the old, especially from certain large peritoneal cells that are found throughout the body. The cut-end of the digestive tract closes, and later new cells develop at its posterior end. An in-turning of ectoderm, in the form of a pit, fuses with the posterior end of the digestive tract and establishes communication with the outside.
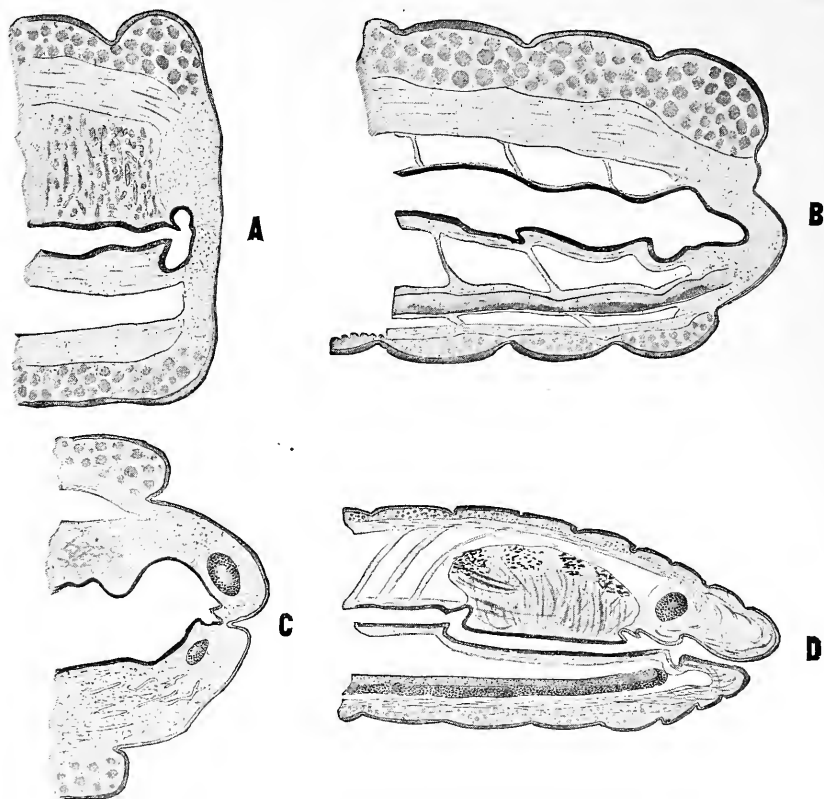


FIG. 58.—After Hescheler. Regeneration of anterior end of earthworm. *A*. After four days. *B*. After eleven days. *C*. After twenty-five days. *D*. After twenty-one days (younger individual).

The regeneration of the anterior end of the earthworm has been carefully worked out by Hescheler, and although on account of the greater complexity of the process the results are not so decisive as those just described, yet in many respects they are in agreement. In Hescheler's experiments only four or five anterior segments were cut off. The closing of the cut-end is somewhat different from that in lumbriculus. A plug of cells soon forms over the end (Fig.

58, *A*).   The new cells appear to be lymph cells.   Although this mass of cells may be quite large, the cells do not seem to form later any of the organs in the new head.   The presence of these cells makes it very difficult to work out the origin of the other cells that appear later.   Owing to the absence of this lymph plug in lumbriculus and nais it is easier to follow in them the regenerative processes.   In the midst of these lymph cells spindle-like cells soon appear whose origin is obscure, but Hescheler thinks it improbable that they are transformed lymph cells, although they are completely intermixed with the latter.   The spindle-cells arrange themselves later in regular bands, that appear to be extensions of the longitudinal muscles.   A few days after the operation, the lymph plug is covered over, beginning at the edge, by the ectoderm.   The new ectodermal cells arise from the old ectoderm, and seem to extend over the lymph plug by a sort of migration process.   Division of the cells does not occur at this time.   These covering cells are at first all alike, the characteristic gland cells of the ectoderm being absent. The digestive tract withdraws somewhat from the outer cut-surface, and its end closes.   The closed end abuts against the inner surface of the lymph plug.   The next changes are initiated by the appearance of karyokinetic divisions in all the tissues of the new part, which lead to a rapid growth and elongation.   Dividing cells are found in the new, as well as at the border of the old, ectoderm, where the new and the old parts are continuous.   At this stage there appears in the lymph plug another kind of cell, that seems to arise, in part at least, from the ectoderm by an in-wandering of new cells.   Other new cells may come from the edge of the old muscles, but it is not clear whether they come from a transformation of muscle cells, or from undifferentiated cells lying in the old muscles.   In addition to these sources of new cells, it appears not improbable that cells may separate from the end of the digestive tract.

Nerve fibres push out from the end of the ventral nerve-cord into the new part, and groups of cells, often in process of division, appear in the old ganglia, even in those that lie a long distance from the anterior end.   It is not improbable, Hescheler thinks, that new cells, as well as fibres, grow forward from the most anterior end of the nerve-cord into the new part.   A mass of nerve cells and fibres appears in front of the old nerve-cord, and extends upwards and around the digestive tract, to meet over the anterior end of the latter in another mass of cells that have arisen from an early in-wandering of ectodermal cells. It is not improbable that the masses around the digestive tract (the commissures) and also the new ventral cord may also include cells that have had the same origin.

A tubular invagination of ectoderm is formed at this time at the

anterior end. It meets the anterior end of the digestive tract ; the two fuse, and the communication of the digestive tract with the outside is established. The pharynx develops from the anterior part of the digestive tract, which after Hescheler's operation may contain some of the original ectodermal stomodæum, since only five of the anterior segments were cut off, and the embryonic stomodæum extends somewhat behind this region. In another experiment, carried out by Kroeber, somewhat more of the anterior end was removed, but the result was the same (Fig. 59), so that it is clear that the new pharynx may be formed from the old endoderm.



FIG. 59. — After Kroeber. Regeneration of anterior end of *Allolobophora fœtida*, after removal of six segments. The first stomodœal invagination had been destroyed. The new pharynx is developing from the endoderm.

Hescheler leaves several points still unsettled, more especially the origin of the cells that give rise to the new musculature, but it is almost impossible to make out their origin in this animal, owing to the presence of the lymph cells. Hescheler's discovery that the cells of the lymph plug do not themselves, in all probability, contribute to the new part, is an important result, and shows that these seemingly undifferentiated cells do not possess the power of giving rise to the different kinds of new tissues. The in-wandering of cells into this solid plug from the ectoderm, and perhaps also from other sources, and their subsequent union to produce the definitive organs, is also a point of capital importance, especially as it puts us on our guard against a too ready acceptation of the view that all cells in a mass that have the same general and undifferentiated appearance have had a similar origin, and in showing that apparently indifferent cells may really carry with them into the new part those characters that determine their fate. Other cells, apparently equally undifferentiated, and lying in the same position, may have quite different possibilities.

In the vertebrates, the regeneration of the tail and limbs of amphibia and of the tail of lizards has been studied by a number of investigators. The regeneration of the tail of several urodeles and of the larva of the frog was investigated more fully by Fraisse

('95) and by Barfurth ('91). If we examine first the results of Fraisse's study of the tail of urodeles, which have bony vertebræ, we find the following changes take place. The cut-surface is covered by the skin bending over the exposed part, accompanied by a migration of cells from the edge of the ectoderm. Only the unspecialized cells leave the old ectoderm to wander out over the cut-surface; gland cells and sense cells are entirely absent from the new ectoderm. These kinds of cells develop later out of the undifferentiated cells over the new part. The development of new vertebræ does not follow the embryonic method of development. In the embryo the endodermal notochord is first laid down, and around this and the nerve-cord mesodermal cells accumulate to form the skeletal tissue. Later the notochord is largely obliterated, as the vertebræ develop, pieces of it being left along the vertebral column. In the regeneration of the tail of the adult animal, the remnants of the old notochord (even if exposed by the cut) do not take any part in the formation of new tissue. In fact, there is no notochord formed at all. From the injured vertebræ, or at least from their covering of skeletal tissue, cells are proliferated, out of which a cartilaginous tube develops, enclosing the new nerve-cord, which is growing out from the cut-end of the old cord. In this tube centres of deposition of calcareous material are formed, and the new vertebræ are produced in this way. The new nerve-cord develops from the cut-end of the old cord, and more especially out of the cells of the lining epithelium of the *canalis centralis*. The new muscles develop from cells that arise from the old muscles.

In the tadpole of the frog the regeneration of the tail takes place essentially in the way just described for the adult urodele, except that, there being only a notochord in the tail, only a notochord is regenerated. According to Fraisse, the new notochord develops from cells that arise from the sheath of the old notochord, and not from the vacuolated cells of the notochord itself. The notochord cells are, he states, derived from the endoderm of the embryo,[1] while the sheath arises from the mesoderm; hence the newly regenerated notochord that arises from the sheath of the old one comes from a different germ-layer. Exception may be taken to this statement, because in the frog's embryo the notochord develops from tissue that is at first perfectly continuous with the mesoderm, and, in fact, may be called mesoderm; also because it is probable, in the light of more recent research, that both the notochord and its sheath have exactly the same origin.

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[1] This seems to be true for urodeles, but whether it is true for the anurans is rather a question of definition, as I have pointed out in my book on *The Development of the Frog's Egg*.

It is known that the tail of lizards breaks off generally at a definite region near the base, and that the break does not occur between the vertebræ, but in the middle of a vertebra — in some species the seventh caudal. The vertebræ are thicker at their ends than in the middle, and are firmly held together by intervertebral cartilages. The centres of the caudal vertebræ are the weakest links in the chain, or at least the place at which the vertebral column is most easily broken in response to the contraction of the tail-muscles.[1] Fraisse and others speak of this arrangement as an adaptation for breaking off the tail.

The new tail that regenerates does not contain a new series of vertebræ, as does the new tail of the salamander, but, instead, a cartilaginous tube that is attached to the half of the broken seventh caudal vertebra.

The regeneration of the new tissues of the tail of the lizard takes place as follows : A scab forms over the cut-surface, composed in part of clotted blood, in part of broken-down tissues from the injured cells. In the course of a week the necrotic tissue falls off, and a smooth surface of ectoderm is found covering the end of the tail. The new ectoderm appears to come from the old, but its method of development has not been studied. The deeper layer of the skin of the lizard is composed of mesodermal connective tissue, and in the new part this layer arises from the connective tissue of the old part. The tissue that forms the cartilaginous tube of the new tail develops from the skeletal tissue of the broken vertebra. The remnants of the old notochord, that are present in the vertebra, have nothing to do with the new structure, nor does the new tube represent in any way a notochord, but it appears to be a structure *sui generis*. In later stages, osseous plates may be formed in the cartilage, but these are too irregular to be compared to vertebræ. A tube grows out from the cut-end of the nerve-cord, which in some forms, as Fraisse shows, is only an extension of the lining epithelium of the nerve-cord. In other forms it is possible that other cells of the old cord may also grow backward, divide, and produce new cells. The fine thread that is formed in this way does not send out any nerve fibres into the surrounding parts. In *Anguis fragilis*, however, a few ganglion cells are present in the new cord. It is probable, Fraisse states, that while the new tube is morphologically a nerve-cord, yet physiologically it is not functional in any of the reptiles.

The new muscles come from the old ones. Fraisse thinks that the new muscle fibres come from the so-called " spindle fibres " that split off from the primitive muscle bundles. These fibres, Fraisse believes, originate normally during the process of physiological regeneration of

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[1] The attachments of the muscles may be the cause of the break in the middle of the vertebræ, rather than between two vertebræ.

the muscles, and also after injury to the muscles. From these spindle cells the new muscle fibres develop in the same way as the muscle cells of the embryo.

Fraisse sums up the results of his studies of regeneration as follows: (1) Both in amphibians and reptiles, injured tissues can only produce new tissues like themselves. The leucocytes assume only the function of nutrition and of devouring the broken-down parts of tissues. They never become fixed tissues — neither connective tissue nor any other sort. (2) All tissues are capable of regenerating themselves, either directly out of their differentiated elements, or out of a matrix. As a matrix for the epidermis, there is the Malpighian layer of the skin; for the central nervous system, the epithelium of the central canal of the nerve-cord; and for the musculature, the spindle fibres.

Fraisse also formulates the following general statements: (*a*) Regeneration is neither a pure recapitulation of the ontogeny nor of the phylogeny. The process is rather a hereditary one, with which complicated adaptations of the tissues are often involved that follow the laws of correlated development. (*b*) We cannot explain the phenomenon of regeneration, as the result of wounding the tissues, or as the outcome of an increase in the food supply, or as due to the removal of a resistance to growth. Far more important are the principles covered by the former paragraph, (*a*).

Barfurth has studied in detail the regeneration of the tail in some amphibia; and his results, while not covering as much ground as do those of Fraisse, yet give a more detailed account of the origin of the new tissues. Barfurth's results on triton and siredon are not essentially different from those of Fraisse. In the tadpole of the frog, Barfurth finds that the notochord regenerates from the sheath of the old notochord. In the larval urodele, he finds that the new notochord arises as in the tadpole, and not from the skeletal sheath, as Fraisse maintains. In very young larvæ of siredon the chordal cells themselves seem to give rise to the cells of the new notochord. In older larvæ, in which the skeletal tissue is developed around the notochord, regeneration takes place both from this tissue and also from the sheath of the notochord. He concludes that in the regeneration of the new notochord, and also of the skeleton, the origin of the cells depends upon the developmental stage of the supporting tissues.

In regard to the regeneration of the muscles, Barfurth comes to the following conclusions: In very young larvæ of siredon, the degenerative changes in the muscle cells are often very slight. Regeneration takes place by growth from and the displacement of the old muscles. During this time bud-like terminal and lateral formations occur in the muscle fibres. These outgrowths contain nuclei and

form sarcoblasts; and these pass into the new part, where they make the new muscle fibres in the same way as do the cells of the embryo. In older larvæ of the frog, and in mature animals in general, the changes are more complicated. Two processes can be distinguished: (*a*) degenerative and (*b*) regenerative. (*a*) Broken-down muscle fibres that have been cut, and torn-off pieces of muscle fibres, are found present. There follows an accumulation of leucocytes and of giant cells. The nuclei in the degenerating muscle fibres atrophy, and the substance of the fibres breaks down. (*b*) The muscle fibres split lengthwise to form spindle fibres, and there is an increase in the number of nuclei at the same time. Sarcoblast-like outgrowths of the old muscle fibres are formed, which produce the sarcoblasts that become new muscle fibres.

Barfurth agrees with Fraisse in two main points, viz. that all the tissues of the tail have the power of regeneration, and that each tissue produces only tissue like itself. The law which Kölliker attempted to establish, viz. that the elements of the formed tissues have lost the power of producing other kinds of tissue, — the law of the specification of the tissue, — is supported by these results of Fraisse and of Barfurth, but is contradicted, as has been shown above, by the results on the earthworm, and also as we shall see even in the amphibia, as for instance in the regeneration of the lens of the eye.

Spallanzani[1] was the first to study the regeneration of the limb in salamanders, and found that the skeleton in the new part is like that in the normal limb. Bonnet, Philipeaux,[2] as well as other naturalists,[3] also examined the regeneration of the limbs of salamanders. Götte ('79) has studied the embryonic development and the regeneration of the limb of triton, especially in regard to the origin of the new bones. He found that the skeleton develops in much the same way in the embryonic limb and in the regenerated limb, and the process in the latter may be said to repeat that in the former. This is especially true for the regeneration of the limb of a very young larva, but the older the larva the more it departs from the embryonic type of development. If the limb is cut off through the upper arm, or through the thigh, new tissue develops over the cut-end. If the larva is quite young, so that formation of the cartilages in the leg has not gone very far, the new tissue differs very little from the old; but if the leg of an older larva is amputated, the difference between the old and the new parts is more striking. If the bones of the leg have

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[1] *Prodromo*, 1768.

[2] Philipeaux, *Comptes rendus de l'Acad. des sciences de l'Institut de France*, Année 1866, 1867.

[3] Todd (*Quarterly Journal of Science, Literature, and Arts*, Vol. XVI), Blumenbach, Treviranus, Von Siebold.

become ossified, the transition from the old to the new part is at first very sharp. The new tissue, that will make the new cartilages of the new limb, develops as a cap over the cut-end of the old bone. Götte does not give an explicit statement in regard to the origin of the new cartilage, but his account leads one to suppose that it develops from the old cartilage or from some part of the bone. This is, in fact, the case, as I have observed in preparations of the regenerating leg of *Plethodon cinereus*, in which the new cartilaginous tissue comes from the periosteum of the old bone. Götte shows that two long rods of tissue are formed, that are separate for the greater part of their length. They give rise to the two bones of the lower leg, or forearm, as the case may be. The broken end of the femur or humerus also completes itself by a short cartilaginous cap, which is at first continuous with the two rods just described. The ends of these two rods break up into a series of pieces that form the tarsalia, or the carpalia, and the digits. Two digits are first formed, and the others are added as outgrowths from the side of one of the two rods. It is important to note that the new cartilages are formed, in large part, out of a continuous substratum (or rather of two) which separates into proportionate parts to produce the elements of the new limb.

The regeneration of the muscles of the limb of an adult animal, plethodon, has been recently worked out by Towle. The leg was cut off in the middle of the forearm. Extensive changes take place in all the muscles that extend across the level of the cut. The old fibres in the lower end of the muscle, *i.e.* those near the cut-end, disintegrate, and the number of nuclei greatly increases. The division of the nuclei seems to be direct, each retaining some of the old muscle substance about itself. From some of these cells the new muscle tissue is formed in the new part. Higher up in the forearm the muscle fibres break down to a smaller extent, and still higher up some of the old fibres may remain intact. New muscle fibres are also formed in the old muscle, especially in the region near the cut-end.

The process of regeneration has not been so fully worked out in any other vertebrates as in those described in the preceding pages, although the regeneration of *single tissues* or organs in the vertebrates has been extensively investigated. In all such cases it is found that like tissues give rise to like.

In the planarians it has been found that during regeneration the ectoderm covers the exposed surface, and from it arises the new ectoderm; the digestive tract appears to come in part from the old tract and in part from the middle-layer cells; the nervous system appears also to develop out of the middle-layer cells that are found scattered through the body. These cells seem to form a sort of reserve supply

that gives rise to the digestive tract, nervous system, and middle-layer cells in the new parts. From them also arise the new pharynx, and the lining of the pharynx chambers, as well as some other structures. It is impossible to say at present whether one and the same kind of cell may give rise to all these structures, or whether different kinds of cells are present in the middle layer, that cannot be distinguished from each other by the methods at present at our command.

The changes taking place in the tissues of those animals that regenerate by morphallaxis have been only quite recently carefully investigated. Bickford stated that in tubularia the old differentiated tissue changes over directly into the tissue of the new part, and Driesch confirmed this statement. Stevens has studied by means of serial sections the different changes that take place. Division of both ectodermal and endodermal cells is found to occur, but especially the ectodermal. Whether all the ectodermal cells divide, or only some of them, is difficult or impossible to state, but whether this happens or not, all the old region goes over into the new hydranth.

The changes that take place in hydra have been recently worked out in my laboratory by Rowley, who finds that a certain amount of division takes place in the old cells, especially in the ectoderm. The division of the cells is not a very active process, and it seems not improbable that many of the old cells go over without dividing into the new part.

One of Trembley's most celebrated experiments was that in which hydras were turned inside out (Fig. 1, *A*, *B*), so that the ectoderm came to line the inner cavity and the endoderm to cover the outer wall. The tentacles were not everted but remained sticking out of the mouth of the everted animal. Their openings, or arm-holes, therefore, appear on the outer surface of the body. In order to prevent the everted hydra from turning itself back again, as it tends to do, Trembley pushed a small bristle crosswise through the wall of the body. Finding the hydras still sticking on the bristles the next day, he concluded that they had not returned to their former condition, but that the outer layer (the endoderm) had changed its character so that it became ectoderm, and the inner layer (the ectoderm) became endoderm.[1] The experiment seemed to show that the two layers could change their specific character and be transformed into each other according to their position in the animal. These remarkable results were not challenged until 1887, when Nussbaum repeated the experiment and showed that Trembley had overlooked an important fact. It was found that even the bristle pushed through the body does not prevent the hydra from regaining its original condition, although it may delay the turning back. If the turning back can be

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[1] How the tentacles could have gotten into their normal position is not explained.

prevented, the animal dies. Nussbaum showed how the turning back takes place in an animal while it remains on the bristle. The everted foot-end begins first to turn back, pushing into the central cavity. When it comes to the bristle it passes to one side of it, and continuing to turn back the foot passes out of the mouth, drawing the rest of the body after it.[1] The last act of the turning can take place only by tearing away through one or both sides, and this is often done. The bristle may still remain sticking to the body through one side, or even remain through both sides if the body has, after tearing through, healed up around the bristle. The process of turning back may take place quite quickly, and had been overlooked by Trembley, who trusted too confidently to the presence of the bristle sticking through the animal.

The method by which the turning back of the layers takes place was not, it appears, clearly described by Nussbaum in his first paper, for his account seems to imply, in certain passages, that the ectoderm may slide over the endoderm during the process, rather than that both layers always turn together. Ischikawa, who studied the problem later, gave a clearer account of the method of turning back. Nussbaum has stated in a later paper that he had described essentially the same process.

In conclusion, it can be definitely stated that a transformation of ectoderm into endoderm cannot take place in hydra. Ischikawa also tried removing the endoderm from a piece by spreading it out and then killing the inner layer by weak acid applied with a brush, but pieces of this sort failed to regenerate a new endoderm.

Tower has recently stated that if a living hydra is put into a strong light from an arc lamp of 52 volt 12 ampere capacity, that is focussed on the animal (after passing through an alum cell), the ectoderm cells fly off, but if the animal is kept, it subsequently produces a new ectoderm. Whether all the ectoderm is lost, or only the larger neuro-muscular cells, was not made out.

One of the most unexpected discoveries of recent times in connection with the problem of regeneration is the renewal of the extirpated 'eye of triton and salamandra. Colucci first discovered in 1891 that if the eye is partially removed a new eye develops from the piece that remains and that *the new lens develops from the margin of the bulb*. Wolff, a few years later, not knowing of Colucci's results, also found that after extirpation of the lens of triton, by making an incision in the cornea, a new lens develops from the edge of the old iris. Wolff pointed out the great theoretical importance of this result. The experiment has been repeated and confirmed by

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[1] The foot sometimes pushes out through one of the slits made by the bristle instead of out of the mouth.

a number of more recent workers, so that there remains no question
as to its accuracy.

After the removal of the old lens the wound in the cornea
quickly heals, and in the course of two or three weeks a thickening
appears at one point at the edge of the iris (Fig. 60, *A*). The cells
that produce this thickening are the ordinary deeply pigmented cells
of the iris, where the outer layer of cells of the iris becomes continu-
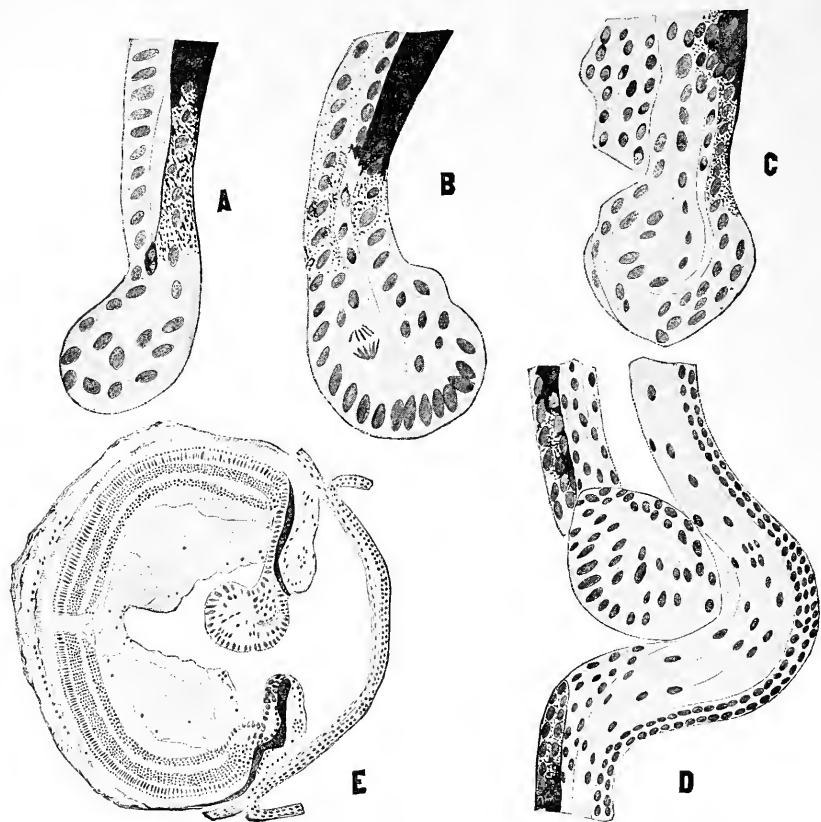


FIG. 60. — After Wolff. Regeneration of lens of eye of Triton. *A.* Edge of iris with beginning
lens. *B*, *C*, *D*. Later stages of same. *E*. After Fischel. Whole eye with regenerating lens.

ous with the inner layer. The cells increase in number and produce
a spheroidal ball that hangs down into the space formerly occupied
by the lens (Fig. 60, *E*). The cells become clearer by absorbing
their pigment and arrange themselves concentrically as in the normal
lens. When fully formed the new lens separates from the iris and
occupies the normal position.

The most surprising fact in connection with the development of

the new lens is that it arises from a part of the body from which the lens of the eye never develops in the embryo of this form or of any other vertebrate. In the embryo the lens develops from the ecto-derm at the side of the head and only secondarily unites with the optic cup, that has come from an evagination of the anterior wall of the fore brain. In the regeneration of the adult lens, however, the ectoderm covering the eye takes no part in the formation of the new lens, — in fact, it is separated from the eye by the thick inner, meso-dermal layer of the cornea. The lens develops, as has been stated, from the already differentiated layers of the iris. It is a point of further interest to notice that the cells that form the transparent lens come from the iris cells that are in part at least filled with black pig-ment. If this pigment remained in the cells the new lens, while it might be structurally perfect, would be physiologically useless. The pigment disappears, however, as the lens develops. In this case we find a highly specialized organ, the lens, developing out of tissue also specialized in another direction. It does not simplify the prob-lem to point out that the lens and the iris are both parts of the eye, since they have arisen from different parts of the body and have only secondarily come into apposition with each other. Colucci was contented to point out that both the embryonic lens and the regen-erated one come from ectoderm and that the result can be brought into harmony with the " germ layer " hypothesis.

Wolff has called attention to the fact that the new lens arises from the upper edge of the iris, and that this is obviously the most advantageous position in which it could develop from the iris, since by its own weight it falls into place as it develops. If the lens had developed from any other point of the margin, its position would be less advantageous, as it might not be brought into its proper position.

Fischel, who has more recently studied the regeneration of the lens in the larvæ of *Salamandra maculata*, finds that after the removal of the lens the iris is thrown into wrinkles or folds and may stick at first to the cut-edge of the cornea. After the cornea has healed, the iris returns to its normal position. He finds that the first changes are more or less alike around the entire rim of the iris and involve a partial absorption of the pigment, a separation of the inner and outer layers at the edge, and a swelling of the margin. These changes go only a little way in those parts that do not pro-duce a lens, but at the upper edge of the iris they go farther and lead to the formation of a lens in that region. He finds also that a new lens develops in animals kept in the dark as well as in those kept in the light, and in the same way.

Fischel also tried the effect of removing a part of the upper edge of the iris at the time when the lens was extirpated, in order to see

if, in the absence of this part, the lens would develop from other parts of the uninjured margin of the iris. He found that the new lens still comes from the upper edge of the iris from the part left after the operation and not from the intact edge in other parts. This seemed to show that an injury to the iris is in itself a stimulus that starts the formation of a lens. This conclusion is made probable by the results of other experiments in which the iris was stuck at several points, when new lenses began to develop at several of these regions of injury. In some cases Fischel found that two or more lenses began to develop when the iris had not been intentionally injured; but it is not improbable that some sort of injury may have been effected when the lens was removed. Fischel, as has been said, removed extensive portions of the upper part of the iris and found that a new lens could be formed at the cut-edge, even in the region of the *pars ciliaris;* and, even after the removal of the entire upper part of the iris, lens-like structures may appear in the inner or retinal layer of the remaining region.

If instead of removing the lens it is displaced by pressing on the cornea until the lens leaves its normal position and comes to lie in the vitreous humor, a new lens develops from the edge of the iris, as though the old lens had been entirely removed from the eye, but in the experiments in which this was done the new lens was not well developed. The result shows that it is not necessary that the old lens be removed from the eye in order to induce the regeneration of a new one, but only that the lens lose its normal position in the eye.

In regard to the stimulus that determines the development of the lens, Fischel agrees with Wolff that gravity has a share in producing the result. The absence of the old lens from its normal position, as well as the wrinkling of the cornea, may also enter in as factors. Fischel takes issue with Wolff as to the interpretation of the result as an adaptation, and states that "the organism always responds to a change of relation in only one way, whose direction is already determined by internal structural relations, without regard to whether the result is adaptive or not. The response follows each stimulus in a way determined by the limited possibilities of the cells. With such a uniformity in the reaction, the idea of a fundamental adaptability cannot be connected, since the reaction that appears to us to be adaptive in a series of complicated changes may be non-adaptive in another series."

Whether Fischel has here really met Wolff's argument is, I think, open to question. It does not alter the result to show that factors already existing enter into the process, so long as the organism is so constructed that just those factors are present that bring about a useful response. That the response may be sometimes imperfect does

not affect seriously the argument — in fact, it makes the case all the more remarkable if these imperfect attempts are in the direction of useful responses. Fischel sums up his conclusions as follows : " It is not necessary, and it is irreconcilable with the facts, to describe the formation of the lens in a teleological sense, and to bring this case forward as a proof of the universal application of a teleological principle. As has been already stated, the facts in regard to this case show much more clearly that the organism reacts to each change always in a manner that corresponds to its limited possibilities without regard to a teleological principle. A planarian, for instance, responds to a stimulus and makes a new head, even when it possesses one or more already ; a tubularian produces a hydranth at its basal end, if this end is freely surrounded by water ; an actinian forms a new mouth on the side of its body, etc.; so also do the cells of the *pars ciliaris*, and the *pars iridica retinæ* differentiate into lens fibres. Working blindly, without respect to the consequences as far as they concern the whole, the one thing only is produced for which the conditions are present that bring about its formation in the cells."

### THE PART PLAYED BY THE " GERM–LAYERS" IN REGENERATION

Our examination of the origin of the tissues and organs in the new parts has shown that in most cases the old tissues give rise to the same kind of tissue in the new part; or in some other cases, as in the nervous system, the regenerating organs arise from the same "layer" as that from which they develop in the embryo. These facts have led many writers to state that the tissues and organs in the regenerated part arise from the same germ-layers as do the same parts in the embryo. It is supposed that ectoderm gives rise to ectoderm, and to those structures that arise from the ectoderm in the embryo, as, for instance, the nervous system, stomodæum, etc. The endoderm is supposed to give rise to endoderm, and to endodermal structures, and the mesoderm to mesoderm and its derivates. So fixed has this opinion become that it is not uncommon to find investigators proclaiming the triumphant success of their results, because they have been able to trace the organs in the regenerated part to the same germ-layers that give rise to these organs in the embryo. Before deciding as to the value of this point of view, let us examine briefly the foundations of the so-called germ-layer hypothesis.

The origin of this hypothesis goes back at least to 1759, when C. F. Wolff maintained his thesis that the digestive tract of the chick exists as a flat, leaf-like structure that subsequently rolls up into

a tube. He thought it probable that other embryonic organs might arise in the same way. His views made at the time no impression on his contemporaries, and lay buried until 1812, when Meckel republished Wolff's work in a German translation. Pander, in 1817, distinguished two layers in the early embryo, a serous and a mucous, and stated that later a third, vascular layer appears between the other two. Von Baer published in 1829 his celebrated memoir on the development of the chick, in which he made out two primary layers in the germ, the animal and the vegetative layer, and held that each of these separates into two to produce the four embryonic layers. Remak, in 1851–1855, gave a more precise description of the germ-layers, and stated that from the innermost layer, the epithelium and glandular cells of the digestive tract arise (including the lining of the glands that open into the digestive tract). From the outermost layer he showed that the integument and sense organs and the nervous system develop, and from the two middle layers develop the muscles, blood, excretory, and reproductive organs. By the term "germ-layers" was meant at this time only that the embryo is formed out of sheets.

Huxley in 1849 pointed out that a medusa is made up of two layers, an outer and an inner, and called attention to their possible equivalency to von Baer's serous and mucous layers. This idea of a resemblance between the layers of an embryo and of an adult of a lower form furnished the starting-point for the more modern formulation of the germ-layer hypothesis. Kowalevsky's work on the development of a number of the lower animals showed that there is present in many forms a two-layered stage, or gastrula, formed by an in-turning of the wall of the hollow blastula. In this way two germ-layers are established, an outer and an inner, that correspond to the ectoderm and to the lining of the digestive tract, or endoderm. While Kowalevsky's work did much toward laying the foundation of the modern study of embryology, he himself indulged in very little of the sort of speculation that came into vogue a few years later. Kowalevsky's discovery of the gastrula stage in the embryos of many different groups has been fully confirmed and extended, but the elaborate speculations that have been built up on this as a basis have gone far beyond the evidence, and, for a time, drew the attention of embryologists away from more important problems. Haeckel took a more extreme position than most of his contemporaries, and assumed that the gastrula stage that occurs in so many of the groups of metazoa corresponds to an ancestral, two-layered adult animal, the gastræa, from which all the higher forms have descended. The presence of the gastrula in the development was interpreted as a "repetition" of this ancestral adult stage. Thus the two primary layers are sup-

posed to have an historical meaning.[1]  Embryologists soon began a search for a similar mode of interpreting the middle germ-layer, or layers, which led, amongst other views, to the formulation of the "gut-pouch hypothesis."  From this point of view the body cavities, or cœlomes, are supposed to have been originally sac-like outgrowths from the digestive tract of an ancestral adult animal.  Later, these cœlome sacs are supposed to have been shut off from connection with the digestive tract — their cavities becoming the body cavities, and their walls giving rise to the mesodermal organs.  The formation of pouches from the walls of the archenteron of the embryo in several groups of animals has been interpreted as a repetition of the ancestral adult animal.

A comparison of the germ-layers in different forms very soon led to an attempt to " homologize " the layers in different animals. If the layers have had historically the same origin, or appear in the same way in the embryos, or give rise to the same organs, they are said to be homologous.  In the absence of a knowledge of the first two of these conditions it is generally considered sufficient, if it can be shown that similar organs arise from a layer, to " homologize " that layer in the two forms.  The study of embryology soon became a search for homologies.  The results led to inextricable difficulties and innumerable contradictions until, a reaction setting in, many embryologists became sceptical in regard to the value of this entire method of study.

The results of a detailed study of the process of cleavage in a number of groups have helped, perhaps, to clear the way for a sounder conception.  It has been found that the cleavage of the egg in members of the groups of annelids, mollusks, and turbellarians is extremely similar — so similar, in fact, that it seems hardly possible that they could be due to chance, especially as the series of cleavages is quite complicated.  The discovery of these similarities led at once to comparison, and comparison to the establishment once more of homologies, and the homologies led again to contradictions, until at present scarcely any two workers agree as to a criterion of homology.[2]  Leaving this question aside, however, and fixing our attention only on the similarity of the process of cleavage, we are justified, I think, in looking for an explanation of the similarity in some sort of an historical connection.  We can eliminate, I think, without discussion the possibility of this type of cleavage representing an ancestral

[1] I have given elsewhere ( *The International Monthly*, March, 1901) a fuller treatment of the gastræa theory from the historical point of view.

[2] It may be pointed out that there may be really several kinds of homology, such as homology due to similar origin of the blastomeres, or to their position, or to their fate, etc. The confusion that has arisen may in part result from the attempt to make homologous parts agree in all points.

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adult animal. So far as the question of descent enters the problem, we can infer with some degree of probability that the groups in question may have come from a common group in which the egg divided in much the same way as we find it dividing at the present time. As a formal hypothesis this view meets with no serious difficulty, since a chain of forms, or a continuous living substance, connects the present animals with those living in the past; and we may assume that the same factors peculiar to the egg of the ancestors are still present in the eggs of their descendants. This sort of explanation gives us no causal knowledge of the way in which the egg divides, nor does it preclude the possibility of new changes coming in that may entirely alter the form of the cleavage. Moreover, since we are dealing with a question of historical probability only, we cannot be certain that the same type of cleavage may not have arisen quite independently in each group.

The argument in favor of the gastrula stage also representing an ancestral larval stage may be admitted as a remote possibility, but on evidence even far less satisfactory than that for the similarities of cleavage being accounted for by a common descent. That this gastrula was ever an adult form we have no means of deciding, even as a matter of probability, and even if this could be made plausible it by no means follows that such an adult stage would become an embryonic stage of later forms. Consequently that part of the germ-layer theory that rests on such a supposed connection cannot be looked upon as much more than a fiction.

But even granting that there is an historical, embryonic [1] connection, its small importance for the scientific problems connected with embryonic development, and budding and regeneration has been shown by a number of recent discoveries, and nowhere more clearly than in the cases of the formation of new individuals by budding. As an example may be cited the method of development of the ascidian from the egg, and by means of buds. The work of Kowalevsky, Della Valle, Seeliger, and Van Beneden on the budding process of ascidians showed that there are some discrepancies between the bud development and the embryonic development. The more recent papers of Hjort, Oka, Pizon, Salensky, Lefevre, and others have shown very clearly that the germ-layer theory is inapplicable to the bud development in this group. The bud arises as a double-walled tube, or rather a tube within a tube, with a space between. The outer tube comes in all cases from the ectoderm of the animal; the inner tube has a different origin in different species. In perophora, didemnum, and clavellina, the inner tube comes from endoderm; in botryllus it arises from the ectoderm of the larval peribranchial or

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[1] That is, one not depending on inheritance through adult forms.

atrial cavity. In all these forms the inner tube gives rise to the new pharyngeal cavity of the bud, while this same cavity comes from the endoderm of the archenteron of the embryo. In the bud embryo the peribranchial space is also derived from the inner tube; hence it is endodermal in the first series, and ectodermal in botryllus. In the egg embryo it is ectodermal. In regard to the development of the nervous system there is some difference of opinion. A number of investigators have found that the new brain arises from the outer part of the inner or branchial tube, which has in most cases an endodermal origin. Seeliger and Lefevre believe the nervous system to arise from mesodermal cells that lie between the two tubes. It appears, nevertheless, that in several forms the brain really comes from the inner tube, which also gives rise to the branchial sac. Therefore, in those cases in which the inner tube is endodermal the brain has the same origin, and in the case in which the inner tube is ectodermal, the brain is ectodermal, but the pharyngeal sac has also an ectodermal origin. There is obviously no definite relation between the origin of these structures in the bud and in the egg embryo.

A similar difficulty is met with in the Bryozoa in regard to the development of the egg embryo and the bud embryo.

Braem, who has made a critical examination of the germ-layer theory,[1] has found it impossible to give a morphological definition of a germ-layer, and has adopted a physiological criterion. He thinks that in whatever way a germ-layer arises, whether by folding, or by delamination, etc., it exists independently of its method or place of origin. A layer is not endodermal because it forms the inner wall of a gastrula, but it is endodermal because it develops into the digestive tract. The germ-layers of different forms are only similarly placed, but whether they are homologous will depend on other things. On this view the inner tube of the ascidian bud that gives rise to both digestive tract and to the nervous system is simply an indifferent layer until it gives rise to these structures. Its cells may be looked upon as indifferent, as are those of the blastula. Thus the difficulty of the morphologist is not solved, but the knot is cut. For Braem the germ-layers are convenient terms, since he rejects any historical significance that they may have, and it is just this side of the question that the morphologist has attempted to work out. While the evidence shows that the germ-layers cannot have any such final attributes as embryologists have attempted to assign to them, and that Braem has called attention to the real and important problems connected with the study of development, yet it may still be admitted without endangering the newer point of view, that there may be also an historical question in connection with the germ-

[1] *Biologisches Centralblatt*, XV, '95.

layers, if not in the sense of a repetition of an ancestral adult gastræa, yet in the sense that similarity in embryonic development may in some cases find its historical explanation in a common descent.

If in the light of this discussion we turn to the phenomena of regeneration, we again find evidence showing that the germ-layer theory fails to apply in all cases. It has been pointed out that in lumbriculus, and in the naids, the new mesoderm is derived from the ectoderm, and does not come from the old mesodermal tissues. The mesoderm of the embryo in annelids is derived from one, and later from two, superficial cells of the blastula,[1] that push in about the time of gastrulation. They cannot, at this time, be referred to one layer rather than to the other. It cannot be affirmed, therefore, that in regeneration, the mesoderm arises from a different layer from that in the embryo, but neither can this be denied. The most important point in this connection is that the new mesoderm comes from the ectoderm that is already differentiated, and not from the mesodermal tissues. It is clear, however, that while the lining of the pharynx in the embryo is ectodermal, it is endodermal in the regenerated part.

It is true that these cases are very exceptional, and that generally the new organs come from similar organs in the old part, but one established exception is sufficient to show that the traditional conception of the germ-layers may be of little value, and since the hypothesis itself, out of which the idea in regard to regeneration from definite germ-layers has been formed, has been proven to be insufficient in other directions, the time is ripe to look for a more secure footing. It need hardly be added that the idea of a supposed necessity for an organ to arise from a definite germ-layer is so empty of all significance that we may well rejoice to be able to set it aside as a naïve view that has had its day. Furthermore, a new series of problems has arisen in connection with the experimental work to be described in a later chapter. If, as seems probable, the question of the germ-layers will be merged into the much broader question of the origin of the specification of the tissues, we can in the future more profitably direct our attention to the experimental evidence that bears on the latter question.

### THE SUPPOSED REPETITION OF PHYLOGENETIC AND ONTOGENETIC PROCESSES IN REGENERATION

It has been claimed that at times ontogenetic, and even phylogenetic, processes are repeated during regeneration. Fraisse, for instance, who advocates this point of view, thinks that it has been

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[1] A small amount of embryonic mesenchyme may come from some of the ectodermal quartettes of the embryo and produce the branching muscles of the head, but not the characteristic muscles of the trunk.

too much neglected, and calls attention to several instances of what he believes to be cases in point. He thinks that Bülow is correct in his comparison between the method of development of the new tissue at the end of the tail in certain naids, and the method of gastrulation and formation of the mesoderm in the embryo. Later results have shown, however, that in several points Bülow's observations are incorrect. The in-turning of ectoderm that Bülow compares with the process of gastrulation is connected with the formation of the ectodermal proctodæum, and is not comparable with the development of the endoderm in the embryo.

Götte also, as we have seen, cites a case of resemblance between the regeneration of the limbs of the salamander and their mode of embryonic development. He finds the resemblances less marked as the animal becomes older. The resemblance is, however, not very close and of a rather general sort, and since the same structures develop in both cases out of the same kind of substance, it is not surprising that there should be some resemblances in the processes. This evidence is counterbalanced by the mode of regeneration of the tail in the adult of certain forms, and in the regeneration of the lens of the eye from the iris.

Carrière finds that the eye of snails regenerates from the ectoderm in much the same way as the young eye develops. Granted that the eye is to come from the ectoderm in both cases, and that the same structure develops, it is not to be wondered at that the two processes have much in common.

The mistake, I think, is not in stating that the two processes are sometimes similar, or even identical, but in stating the matter as though the regenerative process repeats the embryonic method of development. If the same conditions prevail, then the same factors that bring about the embryonic development may be active in bringing about the regenerative processes. In fact, we should expect them to coincide oftener than appears to be the case, but this may be due to the conditions being different in the young and in the adult.

It has been claimed also that in some cases there is regenerated a structure like that possessed by the ancestors of the animal. The stock example of this process is Fritz Müller's result on the regeneration of the claw of a shrimp, *Atypoida protimirum*.[1] Fraisse and Weismann and others have brought forward this case as demonstrative. The animal is said to regenerate a claw different from any of those in the typical form, and one that resembles the claw of another related genus, *Carodina*. The value of evidence of this sort is not above question. Przibram has shown in other crustacea that when

[1] Cosmos, Vol. VII, p. 388.

a maxilliped is cut off a structure different in kind often regenerates, but that after several months the typical structure returns.   Do we find here an ancestral organ that first appears, and then gives way to its more modern representative?   If it *resembled* the maxilliped of any other crustacean, the evidence would, no doubt, be accepted by those who accept the evidence furnished by Müller.   What then shall we say to the case, first discovered by Herbst, in which the eye of certain prawns being cut off, an antenna-like organ regenerates?   Since these antennæ are similar to those possessed by the same animal, shall we assume that it once had antennæ in place of eyes?

Another comparison, that Fraisse has made, is worth quoting as showing how far credulity may be carried.   In the regeneration of the tail of certain lizards pigment first appears in the ectoderm of the new part and then sinks deeper into the layers.   Fraisse found a lizard on Capri in which the tail is pigmented throughout life, and although he did not know whether or not the pigment is in the skin he suggests that this lizard represents an ancestral condition, that is repeated by the regenerating tails of other forms.

Boulenger ('88) pointed out that the scales over the regenerated tail of several lizards have a different arrangement from that of the normal tail, and furthermore, the new arrangement is sometimes like that found in other species.   He claims that this shows that such forms are related, even where no evidence of their relation is forthcoming. That the conditions in the new tail may be different from those in the normal tail is shown by the absence of a vertebral column, etc.; therefore that the scales also should have a new arrangement is not surprising, but the facts fail, I think, to show that there need be any genetic relation between the forms in question.   That the conditions in the new tail might be like those in an ancestral form may be admitted, but this is very different from assuming that the results show a genetic relation actually to exist.   The main point is that, even if the results should be nearly identical, it may be entirely misleading to infer that ancestral characters have reappeared.

In some cases an extra digit or toe may regenerate on the leg of a salamander, and this too has been interpreted as a return to an ancestral condition.   But Tornier has shown, as has been stated, that several additional digits, or even a whole extra hand, may be produced by wounding the leg in certain ways, and these too would have to be interpreted as ancestral, if the hypothesis is carried out logically.   It has been shown by King that one or more additional arms may be produced in a starfish by splitting between the arms already present, and if we accepted evidence of this sort as having any value in interpreting lines of descent we should conclude[1] that

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[1] King pointed out the fallacy of this argument.

the ancestors of the starfish had six, seven, or more arms according to the number that can be produced artificially, etc. Therefore, until further evidence of a more convincing kind is forthcoming, we can safely, I think, decline to accept the results, so far known, as having any value in interpreting the relationships or the descent of the animals.

# CHAPTER XI

## REGENERATION IN EGG AND EMBRYO

NOT only do adult organisms have the power of regeneration, but embryos and larval forms possess the same power, and even portions of the segmenting, and also the unsegmented, egg may be able not only to continue their development, but in many cases to produce whole organisms. Haeckel observed in 1869–1870 that pieces of the ciliated larvæ of certain medusæ, and even pieces of the segmented egg, could produce whole organisms. The more recent experiments of Pflüger ('83) and of Roux ('83) on the frog's egg mark, however, the beginning of a new epoch in embryological study. The explanation of this is to be found, I think, not only in the introduction of experimental methods, but also in the fact that Pflüger and Roux realized the important theoretical questions involved in their results.

Pflüger's experiments were made by changing the conditions under which the egg develops in order to determine what factors control the development. Since these experiments were made with whole eggs, the problems of regeneration were not directly involved in his results, although his conclusions are of great importance in connection with questions concerning the regeneration of the egg. A part of Roux's work dealt directly with the development of a new organism from a piece of the egg or of the embryo. Roux's principal discovery [1] ('88) was that a half-embryo develops from either of the first two blastomeres of the frog's egg, if the other blastomere has been injured or destroyed, but that subsequently the missing half of the embryo is " post-generated." Roux was led to this experiment by his discovery that the plane of the first cleavage of the egg corresponds very often to the median plane of the body of the embryo. [2] This relation suggested that there might be some causal connection between the two phenomena in the sense that the first cleavage plane divides the material for the right side of the body from that of the left side. In a descriptive sense this would be, of course, true if the two planes do really correspond, and if there was no later shifting of material

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[1] Roux's earlier experiments in 1885, in which the unsegmented or segmented egg was stuck and a part of its contents removed, the remaining part making a whole embryo, will be considered in another connection.

[2] This had been first discovered by Newport in 1851.

across the middle line, but whether the two phenomena are causally connected, or are merely due to a coincidence, could only be determined by further experiment. The observations themselves are not beyond question, for the two planes do not always coincide, and may be even
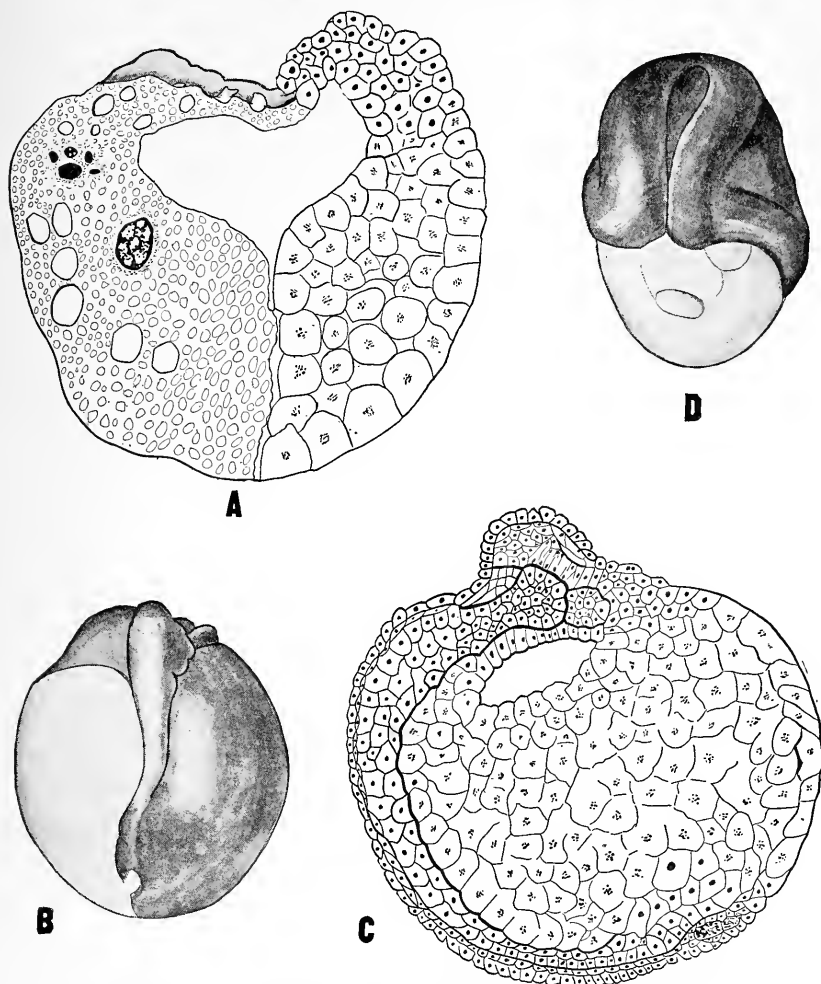


FIG. 61. — After Roux. *A.* Section of semi-blastula of frog's egg. *B.* Half-embryo. *C.* Cross-section of last (reversed right and left in *B* and *C*). *D.* Anterior half-embryo.

ninety degrees apart. These cases of divergence were thought by Roux to be due to an unobserved shifting of the developing embryo, but it is improbable that all cases can be accounted for in this way.

Roux carried out his experiment by plunging a hot needle into one of the first two blastomeres, so that it is injured to such an extent

that its development is prevented. The same needle, without heating again, was used for one or two other eggs, for, if the needle had been so hot in the first instance that both blastomeres had been injured by the heat, this might not happen in the second or the third egg. It was found that amongst the eggs that had been operated upon in this way, some had been so much injured that neither blastomere developed, others had been so little injured that both blastomeres developed, but in the successful operations the uninjured blastomere developed, while the injured one did not. In the last case the uninjured blastomere divided, and produced a large number of cells. A segmentation cavity was present in the upper part of the hemisphere (Fig. 61, $A$). The injured half remained in contact with the other, completing the sphere, but it did not segment. A half-embryo developed from the uninjured half, as shown in Fig. 61, $B$, $C$. This embryo has a half-medullary fold along the side in contact with the injured half. At the anterior end somewhat more than half a head is present, and at the posterior end there is a half-blastopore. The cross-sections[1] (Fig. 61, $C$), through the embryo, show that beneath the half-medullary fold a rod-like notochord is present, which is made up apparently of fewer cells than the normal notochord, but it has, in cross-section, a round and not a half form. At the side, the mesoderm is present, as in the normal embryo, and it has produced the characteristic mesoblastic somites. An archenteron is formed in the half-embryo, and, since it is smaller than the normal, it may, perhaps, be called a half-archenteron. The embryo is, therefore, in most respects a half-structure. The head is, however, nearly a whole head, but whether this is due to a whole head developing out of material derived entirely from one of the two blastomeres, or whether, as Roux supposes, a portion of the material of the injured blastomere has been worked over, *i.e.* "post-generated," remains, I think, an open question.

The results of this experiment seem to confirm Roux's conjecture that the material of each of the first two blastomeres is of such a sort that it gives rise to half the embryo, and, if so, there would be some probability that there is a causal connection between the first cleavage and the separating out of the parts of the embryo. In fact, Roux drew this conclusion, and even attempted to show how such a qualitative division is brought about. It should not be overlooked, however, that this conclusion goes beyond the legitimate bounds of deduction from the results, since the half-development takes place while the injured half retains its connection with the developing half, the former still remaining alive. On the other hand, the presence of the injured half makes the experiment more suitable to demonstrate that each of the first blastomeres gives rise, under normal circumstances, to half of the

[1] The cross-section $C$ is reversed as compared with the half-embryo $B$.

embryo. If one half had been removed, we can foresee that its absence might lead to other complications that would affect the result.

The most important outcome of this experiment is, I think, to show that a half-structure may develop by itself, *i.e.* that there is a certain amount of independent power of development in the parts of the egg.

Roux also tried to show that if, after the second cleavage has been completed, the two blastomeres that lie on opposite sides of the first cleavage plane are killed by a hot needle, the remaining two produce either an anterior or a posterior half of an embryo. An embryo derived from the two "anterior" blastomeres is represented in Fig. 61, *D*. The anterior half of the body is present. Posteriorly the half-embryo abuts against the injured half. It is possible, I think, that this embryo may represent the anterior half of a whole embryo of half size that has been prevented from closing in posteriorly by the mass of injured material of the undeveloped blastomere. Roux did not determine positively whether the two "posterior" blastomeres could give rise to posterior half-embryos; one embryo in his opinion appeared to bear out this interpretation. This part of Roux's work is, it seems to me, not so satisfactory as the part dealing with the first two blastomeres, and we may leave it, for the present, out of the discussion, and consider only the result of the first experiment, in which one of the first two blastomeres was injured. Since the problems involved in the two cases are essentially the same, nothing will be lost by dealing with the first case alone.

The uninjured blastomere first gives rise to a half-embryo. After this has been accomplished, other changes take place that "reorganize," according to Roux, the material of the injured half in such a way that the missing half of the embryo is formed by a process that Roux calls "post-generation." This process can be studied only by means of sectioning the embryos, and since the eggs may be injured to a varying extent, there must be some uncertainty in making out the sequence of events. It is found that the yolk of the injured blastomere is vacuolated in places, and that the protoplasm in the path of the needle has been killed (Fig. 61, *A*). Irregular pieces of chromatin are found in the protoplasm, which seem to come from an irregular breaking up of the nucleus.

The changes that lead to the reorganization of the injured half may take place at different times in different eggs. Roux describes three kinds of reorganization phenomena. The first includes the formation of new cells in the injured half. Nuclei, surrounded by finely granular protoplasm, appear in the protoplasm of the injured blastomere. These nuclei arise from two sources : in part from the scattered chromatin of the injured blastomere itself, and in part from

nuclei, or from cells without walls that have emigrated from the developing half. Around these nuclei, as centres, the protoplasm (with its contained yolk) of the injured half breaks up into cells. This cellulation of the yolk may take place in different eggs at different times. In some cases it may not have appeared as late as the gastrula stage of the uninjured half; in others, it may take place at the time when the uninjured half is segmenting.[1] The formation of the cells in the injured half begins always near the developing half, and extends thence into the injured parts. The new cells are of different sizes, but are larger than those of the uninjured half.

The cellulation of the yolk takes place only in the least injured parts of the protoplasm. Where the protoplasm and yolk have been much injured, they are changed over by the second method of reorganization. This part of the blastomere is either actually devoured by wandering cells, or is slowly changed under the influence of the neighboring cells, so that it becomes a part of these cells.

The surface of the injured half is covered over by ectoderm that grows directly from the developing half (third method of reorganization), — at least this happens where the protoplasm has been much injured. In other parts of the injured half the new cells that have appeared in this part, and that lie at the surface, become new ectoderm.

Post-generation now begins in the reorganized and cellulated half; the cells become changed over into the different layers and organs that make the new half-embryo. A few hours or a night is sometimes sufficient to change a hemi-embryo into a whole embryo. The new half-medullary fold develops from the new ectoderm to supplement the half already present. The mesoblast appears over the side. Its upper part seems to come from the uninjured mesoderm that has grown over to the other side, but this is added to at the free edge by cells that belong to the newly cellulated part. The new differentiation is, in general, in a dorso-ventral direction. The lacking half of the archenteron arises in connection with the half of the archenteron already present in the hemi-embryo. The yolk cells arrange themselves radially, and a split appears in the post-generated part, extending from the archenteron of the hemi-embryo. The split opens, and the new half-archenteron appears. In general, Roux states, the post-generation of the organs of the injured half proceeds from the already differentiated germ-layers of the hemi-embryo. The post-generation begins where the exposed surfaces of the germ-layers of the hemi-embryo touch the newly cellulated regions of the injured half.

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[1] This difference is due, I suppose, to the amount of injury that the nucleus of the injured half may have suffered.

It is most difficult to account for these post-generative changes, since the new part has, according to Roux, a double and even a three-fold origin. The pieces of the old nucleus, he admits, may take a part in the formation of the new cells; wandering cells migrate from the yolk mass of the old half into the new, and the cells of the formed germ-layers may be pushed over to the other side. Since a certain share, and perhaps a large share, of the new cells comes from the hemi-embryo, it is clear that, in addition to the power of self-differentiation shown by the uninjured blastomere, we must also ascribe to it certain *regenerative* powers, at least to the extent that each kind of cell that comes from it can give rise in the injured half to cells like itself, and produce similar structures in the other half.

If then, as Roux supposes, the development of the egg consists in an orderly, qualitative series of changes that lead to the subsequent differentiation, we must also suppose that the new parts are gifted with latent powers by virtue of which they can re-create all parts of the other half. Roux supposes, in fact, that each cell carries with it a sort of reserve-plasm, that is dormant in ordinary development but is awakened when any disturbance of the normal development takes place. Objections have been made to this subsidiary hypothesis, since the addition of this to the original assumption of a series of qualitative changes involves such complications that the view can hardly be considered a probable one. This objection is, I think, not as strong as certain critics believe, since the facts of development show beyond a doubt that although the egg has the power of progressive change it has also, as certain experiments show, the power of reorganization, if the ordinary course of events is interrupted. This admission by no means throws us back upon Roux's hypothesis, for, as will be shown later, a different conception of the development may better account for both phenomena.

Inasmuch as a good deal of discussion has taken place in regard to the process of post-generation described by Roux, it should be stated that Endres and Walter reëxamined the process, and found, as had Roux, that the reorganizing cells migrate from the uninjured to the injured side, and around them the protoplasm of that side makes new cells. They found that the injured half is directly overgrown by the ectoderm from the developing half. When the material of the injured blastomere is only incompletely reorganized, there is formed, after post-generation, an embryo that has a protrusion of yolk in the dorsal part of the body. When the injured material is completely worked over, a perfectly formed embryo may result. The typical half-embryos that Roux obtained were also obtained by Endres and Walter. They deny that whole embryos develop from one of the first two blastomeres, as Hertwig affirms.

Hertwig repeated Roux's experiment and obtained results entirely different from those of Roux. He injured one of the first two blasto-meres of the frog's egg with a hot needle, or by means of a galvanic current. Hertwig states that after the operation the egg turns so that the uninjured part lies uppermost. This is owing, he thinks, to the appearance of a blastula or of a gastrula cavity in the developing
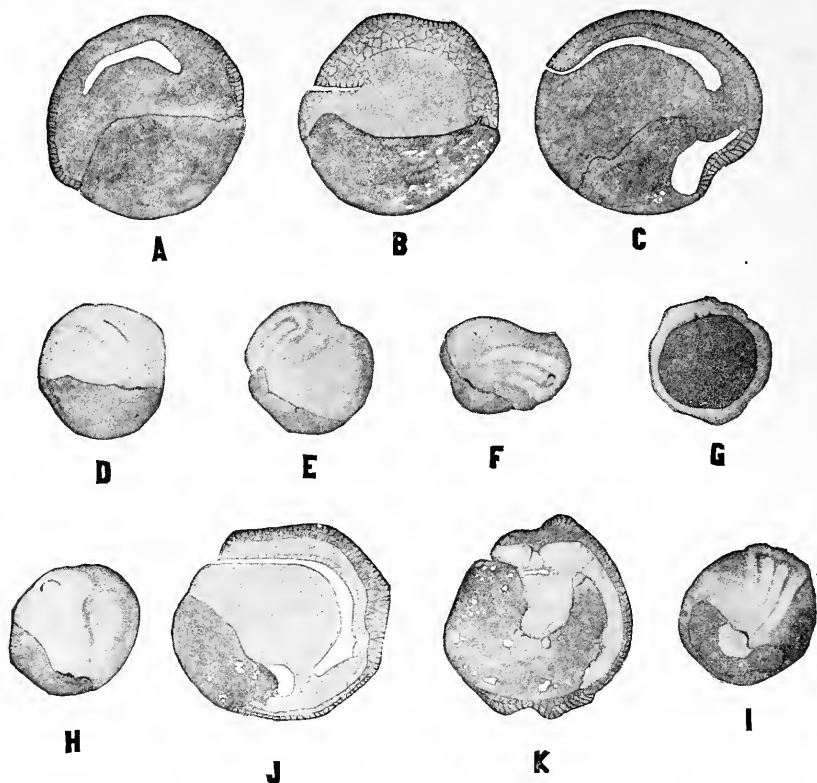


FIG. 62.—After O. Hertwig. *A.* Section through a frog's egg (blastula stage) in which one blasto-mere had been killed. *B.* Same. Gastrula stage. *C.* Later gastrula stage. *D, E.* Surface view of embryos from one of first two blastomeres. *F.* Same as last (*E*). Dorsal view. *G.* Ventral view of last. *H.* Dorsal view of another embryo, lying in a very eccentric position. *I.* Later stage of embryo from one blastomere. Other injured blastomere nearly covered over. *J.* Section through gastrula stage of embryo from one of first two blastomeres. *K.* Cross-section of the embryo shown in *F* and *G.*

part. The segmentation cavity is found in many cases surrounded by the cells of the segmenting half (Fig. 62, *A*), but at other times at the border between the new and the old parts. In still other cases the cavity may lie eccentrically, and in some cases the floor of the cavity may be bounded by the yolk substance of the injured half. An em-bryo appears on the upper, uninjured part, though it is not, according to Hertwig, a half-embryo, but a whole embryo, or at least one approach-

ing that condition (Fig. 62, *D, E, F, G, H*). It is shorter than the normal embryo, and its posterior end is incomplete. When these embryos are cut into sections, it is found that the part that has developed corresponds to the dorsal part of a normal embryo, but the ventral part is continuous with the yolk substance of the injured half (Fig. 62, *B, C, J, K*). Hertwig interprets these embryos as forms in which the yolk portion of the developing half, together with the whole of the injured blastomere, represents a yolk mass that has not yet been enclosed by the margin of the developing part.

In nearly all the embryos that Hertwig has described, the medullary folds appear eccentrically on the developing half (Fig. 62, *D, F, K*), and in some cases they may lie so far to one side that they are situated almost at the edge; and the less development of one of the folds makes the embryo appear almost like the hemi-embryos obtained by Roux. In fact, one embryo seems to have been a true hemi-embryo.

Hertwig attributes the eccentric position of the embryo to the eccentric position of the blastopore of an earlier stage, but he does not attempt to account for the eccentricity of the latter.

It is significant in this connection to find that Hertwig obtained other embryos that show a condition of " spina bifida." In these there is an exposure of yolk in the mid-dorsal line between the halves of the medullary folds. Still other embryos in the same series of experiments were only slightly injured, and developed nearly normally. In these cases, Hertwig thinks, the blastomere that was stuck had been only slightly injured, and had partly developed. I have also often observed in this experiment that the injured blastomere may segment and add cells to the developing half, but in such cases the development of the injured half may be less regular than is that of the uninjured half. It seems to me not improbable that in several of the embryos described by Hertwig both blastomeres have taken part in the development. The main points of difference between the results of Roux and of Hertwig cannot, however, be explained in this way, and the explanation is to be found in another direction.

Hertwig emphasizes the view that the injured blastomere is not dead, but exerts an influence upon the other half — an influence of the same kind as that which the yolk of a meroblastic egg has on the protoplasmic portion of the egg from which the embryo arises. He ventured to prophesy that if the injured yolk mass could be entirely removed, the uninjured blastomere would produce a normal embryo without defect, and one like the normal embryo in every respect except in size.[1]

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[1] The development of isolated blastomeres of the ctenophore egg shows that this need not be the case.

Roux interprets Hertwig's results as due to the sudden partial post-generation of a part of the injured half of the egg. He thinks that a half-embryo had first developed, and then to this there has been
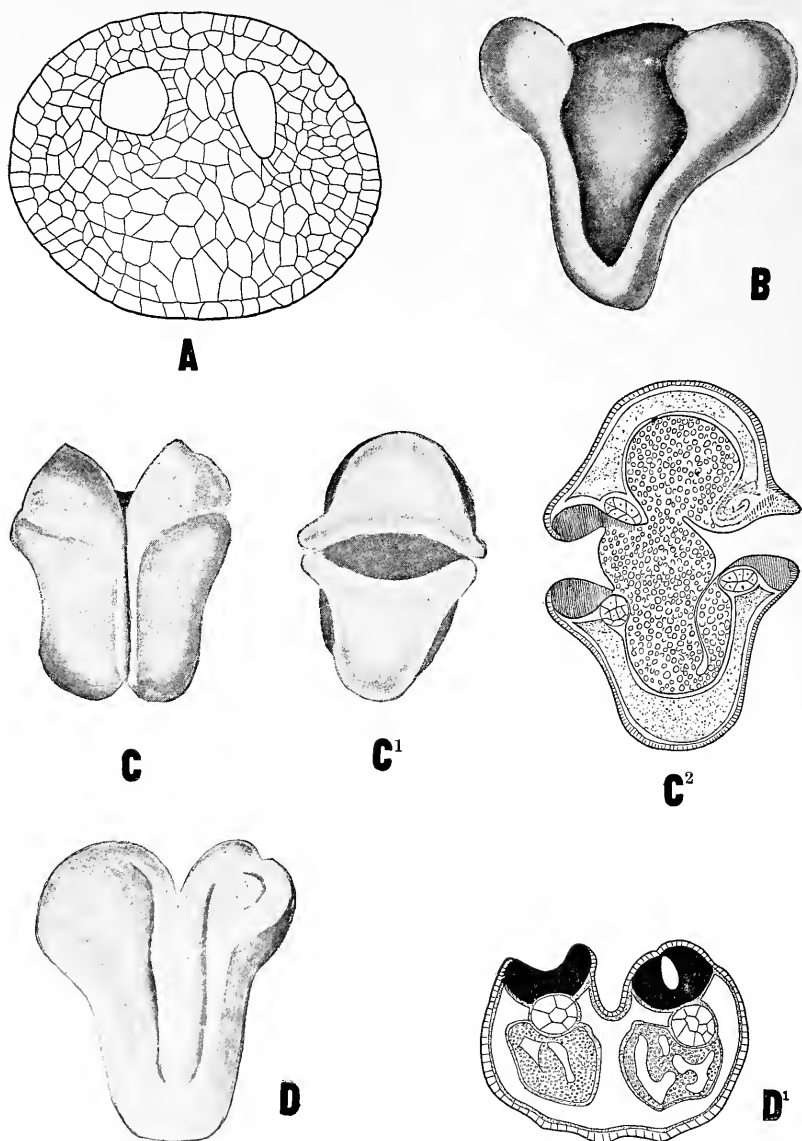


FIG. 63. — *A*. After Wetzel. Section through an egg (blastula stage) reversed at two-celled stage. *B*. After Schultze. Double embryo, from reversed two-celled stage, united ventrally. *C*, *C¹*. Two views of another double embryo (united dorsally). *C²*. Cross-section through last. *D*. After Wetzel. Double embryo united laterally. *D¹*. Section through same.

quickly added a part of the missing side. This reply fails, however, to meet Hertwig's description of the method of development of the embryos. Later work, however, has put us in a position to give a more satisfactory account of the differences between the results of Roux and Hertwig. It seemed to me that the two kinds of embryos might be due to the different positions of the eggs after the operation. It had been shown by Schultze ('94) that if a normal egg in the two-celled stage is turned upside down and held in that position two embryos develop from the egg (Fig. 63, *B, C, D*). These embryos are united in various ways, and arise presumably one from each of the first two blastomeres. These results have been confirmed by Wetzel, who examined more fully into the early development of the twin embryos. He showed with much probability that the proto-plasm rotates in each blastomere, so that in many cases the lighter part flows, or starts to flow, toward the upper hemisphere of the egg. In this way similar protoplasmic regions of the two blastomeres may become separated, and under these circumstances each blasto-mere gives rise to a whole embryo. A cross-section through one of the segmentation stages of one of these eggs is shown in Fig. 63, *A*. The smallest cells are found at the outer side of each half, and the two segmentation cavities lie one in the upper region of each hemi-sphere. Some of the different kinds of embryos that develop from inverted eggs are shown in Fig. 63, *B, C, D*. They are united in Fig. 63, *B*, by their ventral surfaces, and in Fig. 63, *C, C*$^1$, *C*$^2$, by their dorsal surfaces, and in Fig. 63, *D, D*$^1$, at the sides. These differences are probably accounted for by the different ways in which the proto-plasm of the first two blastomeres rotated before the egg divided.

A consideration of these results led me to carry out the following experiment on eggs operated upon by Roux's method. After stick-ing one of the first two blastomeres, some of the eggs were placed so that the uninjured blastomere kept its normal position, *i.e.* with the black hemisphere upward. Other eggs were turned, so that more or less of the white hemisphere was upward. From the two kinds of eggs two kinds of embryos were obtained. From those with the black hemisphere upward the embryo was a half-embryo like that described by Roux, while from the eggs with the white hemisphere upward embryos developed that were in many respects whole embryos of half size.[1] The explanation of this difference will be obvious from what has been said. When the *black* hemisphere is uppermost the contents of the uninjured blastomere remain as in the normal egg, and a half-embryo results. When the *white* hemisphere is uppermost the contents of the uninjured blastomere rotate, so that it generally shifts its relation to the protoplasm in the other injured half, and a

[1] In one case a half-embryo resulted.

Q

whole embryo develops, as in Schultze's experiment.   In one case I obtained a half-embryo from an inverted egg.   The result did not appear to be due to a lack of rotation of the protoplasm, because the medullary folds were white, showing that the protoplasm must have changed its position.   The result can possibly be explained as due to the protoplasm rotating in each blastomere along the line between the halves, so that it still retains the same relation as that of the normal two-celled stage.

The whole embryos of half size are generally imperfect in certain respects on account of their union with the other half.   They resemble in all important points the embryos described by Hertwig, and I see no grounds for interpreting them as embryos of a meroblastic type, but rather as whole embryos of half size, whose development posteriorly and ventrally has been delayed or interfered with by the presence of the other blastomere.

It has not been possible to separate the first two blastomeres of the frog's egg, for if one is removed the other collapses.   In the sala-mander, that has a mode of development similar to that of the frog,[1] it has been possible to separate the first two blastomeres.   Herlitzka, who carried out this experiment, found that each blastomere gives rise to a perfect, whole embryo of half size.   We cannot doubt, I think, that the same power of producing a whole embryo is also present in each of the first two blastomeres of the frog's egg.   When the two remain in contact in their normal relation to each other, each produces only a half ; when like regions of the two blastomeres are separated, each produces a whole embryo.   Thus we see that whatever the fac-tors may be that determine the development of a single embryo from the egg, still each half, and perhaps each fourth also, has the power of producing a whole embryo.

In later papers Roux has stated that he had also, even in his earlier experiments, found other kinds of embryos than the half-em-bryos that he described.   Some of these were whole embryos that had developed from the uninjured blastomere without the injured one taking any part or only a very small share in their formation.   He found, he states, all stages between those embryos that had used up all the yolk material of the injured side (though post-generated) and those that had not used any part of it.   The latter kind of embryo does not recognize as a whole embryo of half size in the sense that a single blastomere has developed directly into a smaller whole embryo, but he believes that there must have been formed at first a half-blas-tula, half-gastrula, half-embryo, and that the last stage completed itself laterally without using any material from the injured half.

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[1] The plane of the first cleavage has been shown in two urodeles to correspond, not to the median longitudinal plane, but to a cross-plane of the embryo.

That the uninjured blastomere may at first segment as a half is not improbable, but that whole embryos are formed only by the formation of new material at the side of a half-embryo is, I think, hardly possible, since the results of Schultze, Wetzel, Hertwig, and myself show that a whole embryo may develop *directly* out of the material of a single blastomere.

Spemann (1900) has carried out some novel experiments on the eggs of triton, and has shown how in another way double structures may be produced. If a ligature is tied loosely around the egg at the first cleavage exactly along the division plane between the first two blastomeres, it will be found later that the long axis of the single embryo lies, in the great majority of cases, across the ligature, and only in a small percentage of cases does the median plane correspond with that of the ligature, and, therefore, with the first cleavage plane.

If one of the latter eggs is allowed to develop to the blastula stage, and the ligature is then drawn tighter, so that the blastula is completely constricted, an embryo develops from each half.

If one of the former eggs is allowed to develop to a stage when the medullary plate is laid down, but is not yet sharply marked off, and the ligature is then tightened, there will be formed (the plane of constriction being across the medullary plate) from the anterior part a normal head with eyes, nasal pits, ears, and a piece of the notochord, and from the posterior part there will be formed, at its anterior end, another new head just behind the ligature. Ear-vesicles develop in this part at the typical distance from the anterior end. The brain that develops has a typical cervical curvature, and eye evaginations appear at the anterior end. The chorda, that extended at first to the anterior end of this region, is partially absorbed.

If the ligature is drawn tighter at a later stage, when, for instance, the medullary plate is plainly visible but is still wide open, a different result is obtained. The posterior part no longer forms a new head at its anterior end, but develops into those structures that it would form normally. In some cases it was found that the region from which the ear develops had been pinched in two, and in consequence a small vesicle appears in front of the constriction and another behind it.

In those cases in which the ligature lies in the median plane of the embryo, it is found that a double anterior end is produced. As the embryo develops it tends to elongate, and in consequence the material is pushed forward on each side of the ligature. A double head is the result. The extent of the doubling depends on the depth of the constriction between the halves. In the most extreme cases two complete heads are formed with an inner nasal pit, eye, and ear on each head, as well as the normal outer ones. The results show that even such complicated structures as the eyes and ears, etc., may arise

from parts of the body where they never appear under normal conditions.

A series of experiments that have been made on the eggs of sea-urchins has led to equally important results. The earliest experiments are those of O. and R. Hertwig, who, in addition to studying the effect of different drugs on the developing egg, found that fragments of the eggs of sea-urchins, obtained by violently shaking the eggs in a small vial, could give rise, if they contained a
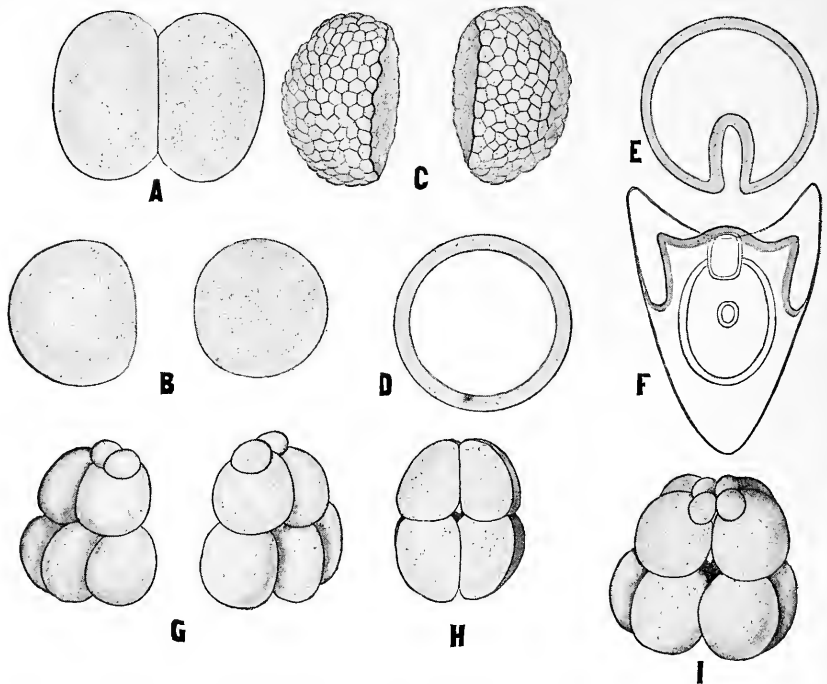


FIG. 64. — Sea-urchin egg and embryo. *A.* Two-cell stage. *B.* Same, with blastomeres separated. *G.* Two half-sixteen-cell stages. *C.* Open half-blastula stages. *D.* One of last, later stage, closed blastula of half size. *E.* Gastrula of half size. *F.* Whole pluteus of half size. *H.* A half-sixteen cell dividing in same way as a whole egg (eight cell). *I.* Whole egg at sixteen-cell stage.

nucleus, to small whole embryos. Boveri made the important discovery in 1889 that if a non-nucleated piece of the egg of the sea-urchin is entered by a single spermatozoon, the piece develops into a whole embryo of a size corresponding to that of the piece. Fiedler, in 1891, separated the first two blastomeres by means of a knife, and found that the isolated blastomere divides as a half, but he did not succeed in obtaining embryos from the halves. Driesch has made many experiments, beginning in 1891, with the eggs and embryos of the sea-urchin. He separated the first two blastomeres ('91) by means of

Hertwig's method of shaking the eggs, and studied the development of the isolated blastomeres. He found that the cleavage was strictly that of a half, and not like that of a whole egg. The normal egg divides into two, four, and eight equal parts. At the next division, four of the cells divide very unequally, producing four very small cells, the micromeres, at one pole. The four cells of the other hemisphere divide equally (Fig. 64, *I*). The isolated blastomere divides at first into two equal parts, then again into equal parts. At the next division two of the cells produce micromeres and two divide equally (Fig. 64, *G*). This is exactly what happens at this division in each half, if the blastomeres are not separated. In later stages a half-sphere is formed that is equivalent to half of the normal sphere (Fig. 64, *C*). The open side corresponds to the side at which the half would have been united to the other half. Thus up to this point a half-cleavage and a half-blastula have appeared.[1]

In later stages the open half-blastulæ close in, producing a whole sphere that becomes perfectly symmetrical (Fig. 64, *D*). A symmetrical gastrula develops (Fig. 64, *E*) by the invagination of a tube at one pole, and a symmetrical embryo is formed (Fig. 64, *F*) that resembles the normal embryo except in point of size.

Driesch has also found that a number of twin embryos arise from the shaken eggs. They arise from eggs whose blastomeres have been disturbed or shifted, so that each produces a small whole embryo, the two embryos being united to each other in various ways.

In a second paper, published in the following year, Driesch extended his experiments, and attempted to discover how far the "independence" of the blastomeres extends; *i.e.* he tried to find out if all the blastomeres resulting from the cleavage are alike. When one of the first four cells is separated from its fellows by shaking, it continues to divide, in most cases as a quarter, and produces later a small spherical blastula. Many of these blastulæ, although apparently healthy, never develop further, although they may remain alive for several days. In one experiment only eight out of twenty-six reached the pluteus stage, with a typical digestive tract and skeleton.

From these experiments Driesch drew the important conclusion that the cleavage cells or blastomeres of the sea-urchin's egg are equivalent, in the sense that if they were interchanged a normal embryo would still result. A somewhat similar view is expressed in the dictum that the position of a blastomere in its relation to the others determines what part it will produce, if its position is changed it gives rise to another part, etc., — or, expressed more concisely, the

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[1] In some cases, especially in sphærechinus, even at the eight-celled stage, the blastomeres seem to shift their position, so that a whole sphere of half size is formed.

prospective value of a blastomere is a function of its position.[1]
Driesch extended these experiments further in 1893. His aim was
to separate different groups of cells at the sixteen-cell stage in order
to see whether the cells around the micromere pole (or "animal pole ")
if separated from those of the opposite (or " vegetative pole ") could
produce a whole embryo, etc. Eggs whose membranes had been re-
moved by shaking immediately after fertilization were allowed to
develop normally to the sixteen-cell stage and were then shaken into
pieces. Amongst the groups of cells that were present those that con-
tained the micromeres were picked out. It was found that they give
rise to whole embryos. In order to obtain cells that belong to the
vegetative hemisphere, the blastomeres were shaken apart at the
eight-cell stage, and those groups of cells that in later divisions did
not produce micromeres were isolated. From these also whole em-
bryos develop. The results show that the cells of both hemispheres
are able to produce whole embryos, and that at the sixteen-cell stage
the different parts of the egg are still capable of producing all parts
of the embryo. It is important to observe that the results of the
experiment do not show that if the normal development goes on
undisturbed any part of the egg may become any part of the em-
bryo, for it is highly probable that a definite region of the egg may
always produce a definite part of the embryo. The results do show,
however, that, even if this is true, any cell has the power of produc-
ing any or all parts of the embryo if the normal conditions are
changed.

In connection with these experiments Driesch discussed the fac-
tors that determine the axial relations of the embryo. If all the cells
have the power of producing all parts, what determines in the normal
development, and also in the development of a part of the whole, the
axial relations of the embryo? Driesch assumed that the egg has a
polar structure, and that the same polarity is found in all parts of the
protoplasm. Around this primary axis all the parts are alike or
isotropous.[2] The origin of the mesenchyme and the position of the
archenteron, that develop at one pole, are determined by the polarity
of the protoplasm. The plane of bilateral symmetry may appear in
any one of all the possible radial planes around the primary axis.
The selection of a particular one is due to some accidental difference
in the structure of the protoplasm, or to some external factor. In
later papers Driesch modified this view, and assumed that along with
the primary polarity a bilateral structure also exists in the proto-
plasm.

[1] Hertwig had a year before expressed a similar view in regard to the equivalency of the
blastomeres.

[2] A view advanced by Pflüger.

Wilson ('93) studied the development of isolated blastomeres of amphioxus, and found that it agreed in all essential respects with the mode of development of the blastomeres of the sea-urchin. The isolated blastomeres of the two-cell and four-cell stages produce whole embryos, but the blastomeres of the eight-cell stage develop only as far as the blastula. The blastomeres segment, after separation, in most cases not as a part, but as a whole egg would divide, although the cleavage of the one-eighth blastomere only approaches that of the entire egg, but is never identical with it. Incompletely separated blastomeres give rise to twins, triplets, etc. Wilson agreed with the Hertwig-Driesch conception of the value of the early blastomeres, and accepted the view that the fate of each is a function of its position, and that at first they are qualitatively alike. During the early cleavage he supposed that a change takes place that is slight at the two-cell stage, greater at the four-cell stage, and in the eight-cell stage the differentiation has gone so far that the blastomere can no longer return to the condition of the ovum. " The ontogeny assumes more and more the character of a mosaic work as it goes forward."

Loeb ('94) showed that if the eggs of the sea-urchin are placed in sea water, diluted by distilled water, the egg swells and bursts its membrane, so that a part of its protoplasm protrudes. Into this protrusion some of the first-formed nuclei pass, and from both the part remaining in the egg membrane, as well as from the protruding part, an embryo is produced, the two embryos often sticking together. In several cases two to eight separate groups of blastomeres are formed from one egg and develop into whole embryos.[1]

The question of the number of cells which are produced by the one-half and one-fourth embryos had not up to this time been determined. Until this was known it could not be stated whether the smaller embryos were miniature copies of the normal embryos in all respects, or whether they assumed the typical form with fewer cells. I found ('95) that the blastula from one of the first two blastomeres contains half the number of cells produced by the whole embryo, and that in the later stages also it contains only about half the normal number. The one-fourth blastomere produces only a fourth of the whole number of cells, and yet can develop with this number, in many cases, into a whole embryo. The one-eighth blastomere produces one-eighth the normal number of cells. In most cases I found that these one-eighth blastomeres do not produce embryos, but occasionally they produce a gastrula, and probably a young pluteus stage.

[1] The evidence to show that more than four and certainly more than eight such groups that come from a single egg can produce a pluteus is, I think, insufficient, and the result improbable.

The development of nucleated fragments of the egg was also studied in order to find out if they too produce a smaller number of cells than does the whole egg, and a number in proportion to their size. The problem is different in this case, because the nucleus has not divided before the piece is separated, and the results ought to show whether there is a prescribed number of divisions for the egg nucleus, or whether the number of times it divides is regulated by the amount of the protoplasm. It was found that the number of cells produced by each fragment is in proportion to the size of the piece. This shows that the division of the nucleus is brought to an end when the protoplasm has become subdivided to a certain point.

A further examination of the number of cells that are invaginated in these smaller "partial" larvæ to produce the archenteron seemed to show that they often use relatively more than their proportionate number. The normal blastula of *Sphærechinus granularis* contains about five hundred cells and turns in fifty cells, or one-tenth the total number. The one-half and one-fourth embryos, and some of the small embryos from the egg fragments, seemed to invaginate more than one-tenth of their total number of cells.

Driesch (1900) reëxamined this point, and found that the embryos from isolated blastomeres may use the proportionate number of cells. I have made a new study of the problem on a larger scale and have found that my earlier statement, as well as that of Driesch, is substantially correct, and that the difference that we found is due to the time at which the embryos gastrulate. Thus the one-half embryos and even the one-fourth embryos, that gastrulate as soon as (or only a little later than) the normal, whole embryos, turn into the archenteron about one-half and one-fourth the number of cells invaginated in the whole embryo; but those partial embryos that gastrulate later (as most of them do) turn into the archenteron more than a half or a fourth of the number of cells turned in *at first* by the whole embryo. This difference between the early and the retarded partial embryos is in large part due to a slow increase of cells that takes place during the delay in development.

Driesch ('95) found that pieces of the blastula wall of the sea-urchin, *if large enough*, can also produce a gastrula and embryo. I found that the number of cells in these pieces does not increase appreciably after they are cut off (if the operation has been carried out at the end of the cleavage period), and that the new embryo is organized out of the cells present at the time of removal of the piece from the wall. There is, therefore, in this case no chance for "post-generation" by means of new cells produced at the side, which Roux has supposed to take place in the frog embryo.

The development of pieces of the blastula wall, if they are not too

small, also shows that the lack of power to develop, found in some of the one-fourth and in many of the one-eighth blastulæ, is not the result of any special differentiation that they have undergone during the cleavage period, but is due to their size.

A recent series of experiments by Driesch (1900) on the development of isolated blastomeres of the sea-urchin's egg has given more exact data in regard to their limit of power to produce embryos, and has shown the possibilities in these respects of different parts of the egg. By means of a method discovered by Herbst (1900) it is possible to obtain isolated blastomeres more readily than by the somewhat crude shaking process. If the eggs, after fertilization and after the removal of the membrane by shaking, are placed in an artificial sea water, from which all calcium salts have been left out, the eggs divide normally, but the blastomeres are not held firmly together, and readily fall apart if the egg is disturbed. By means of a fine pipette any desired blastomere or group of blastomeres can be picked out. If these are returned to sea water they continue to develop.

Driesch found that the one-half and one-fourth blastomeres develop into proportionate gastrulæ and larvæ ; that the one-eighth blastomeres, both of the animal and the vegetative hemispheres, sometimes produce gastrulæ, and even the beginning of the larval stage with the rudiments of a skeleton. There are certain differences between the one-eighth larvæ that come from the animal hemisphere and those from the vegetative half. More of the one-eighth blastomeres from the animal part of the egg die than from the opposite part, but of those that remain alive a larger percentage reach the gastrula stage than in the case of those from the vegetative pole ; their protoplasm moreover is not so clear as is that of the larvæ from the other hemisphere. These "animal pole" blastomeres develop faster than those of the other sort. The gastrulæ from the one-eighth blastomeres of the vegetative hemisphere do not die so often after separation, the protoplasm of the larvæ is clearer, and they often produce long-lived blastulæ with long cilia. The blastulæ often develop into gastrulæ without mesenchyme. These results show that although whole larvæ may be produced from the one-eighth blastomeres of both hemispheres, yet there are certain characteristics that may be referred with great probability to differences that are present in the protoplasm of the two hemispheres of the egg. The differences are not in all cases sufficient to interfere with the production of all the characteristic structures of the embryo, yet traces of the origin of the larvæ can be found in their structure. It is probable that the so-called animal (or micromere) pole corresponds to that part of the egg from which the archenteron is produced. Hence the one-eighth blastulæ from this hemisphere gastrulate

sooner and in proportionately larger numbers than do those from the opposite hemisphere. The vegetative hemisphere would correspond to that part of the egg from which the wall of the normal gastrula is derived, and this may account for the clearer protoplasm of these embryos, their inability in many cases to gastrulate, their larger cilia, and the absence of mesenchyme in some of them. Driesch finds that the number of cells that go into the mesenchyme of the partial larvæ is in proportion to the total number, and that the number of cells in the archenteron is probably also proportionate.[1]

The smallest blastomeres that produce gastrulæ are the one-sixteenth products. Out of a total of 139 cases only 31 produced true gastrulæ, 5 produced gastrulæ with evaginated archenteron, and 103 remained blastulæ with long cilia. The one-thirty-second blastomeres were not observed to gastrulate.

Driesch ('95) has also made a study of the potentialities of the blastula and gastrula stages of sphærechinus, echinus, and asterias. If a blastula is cut in half before the mesenchyme cells are produced, both pieces produce gastrulæ and larvæ. Since some of the pieces probably come from the animal hemisphere, and others from the vegetative hemisphere, it follows that all parts of the blastula possess the power of producing whole embryos, and in this respect the potentialities are the same as for the blastomeres. If the experiment is made at a stage just before the archenteron has begun to develop (Fig. 65, *A*), the results may be different. A half that contains the region from which the archenteron is about to develop will produce a gastrula and a larva (Fig. 65, *A*, lower row to right of *A*). A half that contains only the opposite regions of the egg (Fig. 65, *A*, upper row) may in some cases gastrulate,[2] often abnormally, but as many as half of the pieces do not gastrulate. They may remain alive for a week or more, and even produce a typical ciliated ring with a mouth in the centre, but do not form a new archenteron. These important results show that after the formation of the mesenchyme and archenteron at one pole, the other cells of the blastula wall are no longer able to carry out a process that the same cells were able to carry out at a slightly younger stage, but whether this loss of power is connected with the previous formation of the archenteron, or due to some other change which has by this time taken place in the cells, cannot be determined from the experiment. It is also important to note that these small ectodermal blastulæ can still develop whole, typical, ectodermal organs, the ciliated ring and the mouth, and that the former especially has the characteristic structure of the whole normal ring.

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[1] Driesch's figures seem to show, nevertheless, that the archenterons are proportionately too large.

[2] These may be pieces that were cut obliquely, as Driesch suggests, so that they contain a part of the archenteric region.

Similar phenomena have been made out by Driesch in the development of the archenteron of the same forms. At the end of the nor-
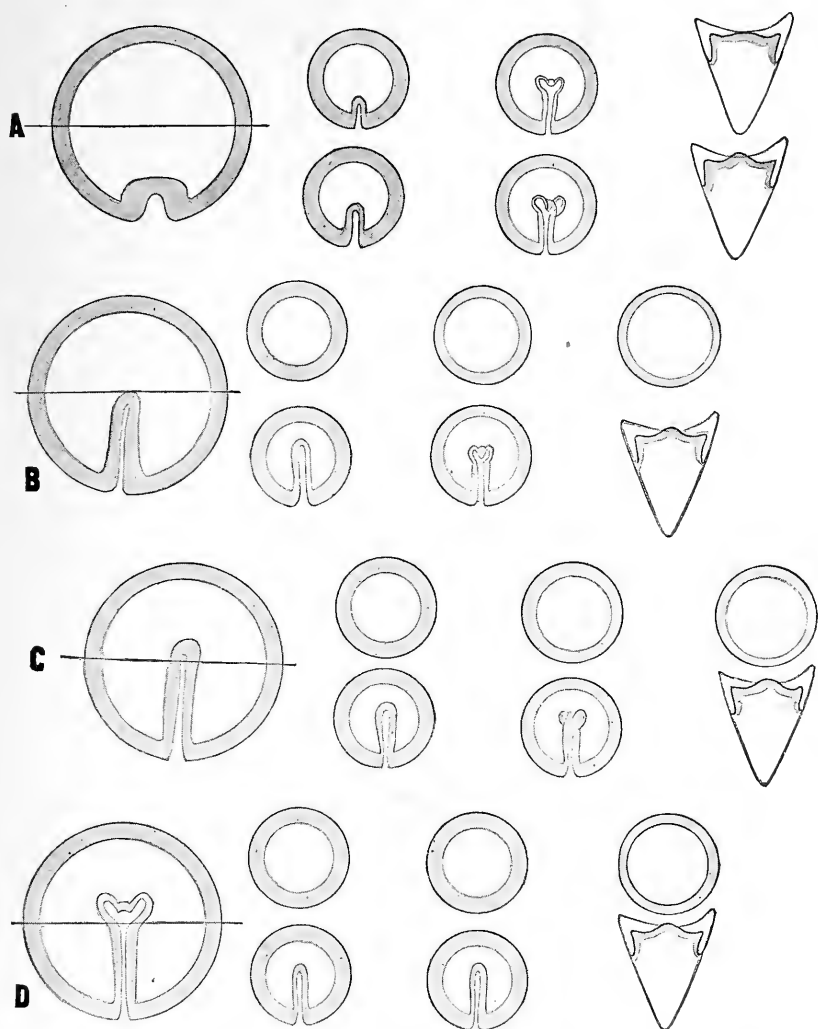


FIG. 65. — *A*. Blastula of sea-urchin beginning to gastrulate. Cut in half as indicated by line. Two rows of figures to right show development of upper and lower halves. *B*. Later gastrula cut in half. Two rows of figures to right show later development. *C*. End of gastrulation process. Embryo cut in half. Two rows of figures to right show later stages of each half. *D*. Formation of endodermal pouches from inner end of archenteron. Embryo cut in two. Two rows of figures to right show later stages.

mal gastrula period of the starfish embryo, there is produced from the inner part of the archenteron two outgrowths, or pouches, that later constrict off to give rise to the cœlom sac and water-vascular system.

If the gastrula is cut in two in such a way that the inner end of the archenteron, *i.e.* the part from which the pouches develop, is cut off (Fig. 65, *C*), it is found that the piece containing the posterior part of the archenteron closes in, forms a new sphere, and from the present inner end of the archenteron (that has also healed over) a pair of pouches is produced (Fig. 65, *C*, lower row to right of *C*). These pouches have arisen, therefore, from a more posterior part of the archenteron than that from which the pouches normally arise.

If the same experiment is made at a later stage, when the pouches have been given off from the archenteron (Fig. 65, *D*, lower row to right of *D*), no new pouches are formed. This means that after the archenteron has once produced its pouches it loses throughout all its parts the power to repeat the process, although these parts possessed this power at an earlier stage. It is a very plausible view that the result is directly connected with the formation of the normal pouches, although it is of course possible that some other change has taken place in the archenteron that prevents the formation of the pouches.

In order to give as nearly as possible a consecutive account of the experiments on the eggs of the frog and of the sea-urchin, a number of other discoveries have been passed over. Let us now examine some of the results on other forms.

Chabry, as early as 1887, experimented with the eggs of an ascidian. By means of an ingenious instrument he was able to prick and kill individual blastomeres. The results of his experiments were not described very clearly, and later writers have interpreted his results in different ways.[1] Chabry stated that he obtained half-embryos from one of the first two blastomeres, but his figures show, especially in the light of later work, that the embryos were whole embryos of half size, although certain organs, as the papillæ and the otolith, may be lacking.

Driesch ('95) reëxamined the development of isolated blastomeres in one of the ascidians, *Phallusia mammalata*, and found that the cleavage of blastomeres, isolated by shaking, is neither like that of the whole egg, nor is it like that of half the normal cleavage, although it shows some characteristics of the latter. A symmetrical gastrula is produced, and from this a typical whole larva of half size. These larvæ lack, however, one or more papillæ, and the otolith rarely develops. The absence of these organs Driesch ascribes to the rough treatment that the egg has received, since embryos from whole eggs may sometimes lack these organs if the development has taken place under unfavorable conditions. The isolated one-fourth blastomere may also produce a whole larva.

Crampton ('97) has also studied the development of the isolated

[1] Driesch, Hertwig, Roux, Weismann, Barfurth. For review see Driesch ('95).

blastomeres of another ascidian, *Molgula manhattensis*. He has more fully worked out the cleavage, and finds that the isolated blastomere segments as a part, *i.e.* as it would have segmented had it remained in connection with the rest of the egg. In general appearance the half-cleavage seems to differ from the half of the complete cleavage, because rearrangements of the blastomeres occur, but despite these shiftings the form of the division is always like that of a part. A whole embryo develops, although there may be defects in certain organs, which are due, he suggests, to the smaller amount of material available for the development of the larva.

Zoja showed in 1894–1895 in a number of jellyfish that the isolated blastomeres produce whole larvæ of smaller size.[1] In one form, liriope, the endoderm that forms the digestive tract is normally delaminated at the sixteen-cell stage, each cell of the blastula wall dividing into an inner and an outer part. In the blastula from the one-half blastomere this delamination also takes place when sixteen cells are present, and not at the preceding cleavage when only eight cells are present. In this form, therefore, the whole number of cells develops before the delamination takes place, and the one-half larva is composed of the same number of cells as is the normal embryo at this stage, but the cells are only half as large. In other species the endoderm appears to begin to develop in the half-larvæ when only half the total number of cells is present.

The conditions in the egg of the bony fishes are very different from those in the preceding forms. The protoplasm, from which the embryo is produced, accumulates at one pole to make the blastodisc. After the cleavage of this blastodisc, the blastoderm that has resulted grows over the yolk sphere at the same time that the embryo is forming along one meridian. I carried out some experiments, in 1895, on the eggs of *Fundulus heteroclitus*. If one of the first two blastomeres of the egg of fundulus is destroyed, the remaining one produces a whole embryo. If three of the first four blastomeres are removed, the remaining one may produce a whole embryo of small size. The problem of development is, in the case of the fish, different from the other cases described, inasmuch as the whole yolk sphere is left attached to the remaining blastomere and is covered over by cells derived from this blastomere. The smaller embryo that is formed lies on a yolk of full size.[2]

Wilson's work on amphioxus has been already described in con-

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[1] Bunting ('94) also found that isolated blastomeres of hydractinia make whole embryos.

[2] If the yolk of the dividing egg is partially withdrawn without disturbing the blastomeres, the form of the cleavage may be altered, but a normal whole embryo develops over the smaller yolk sphere.

nection with the experiments on the sea-urchin's eggs. Later I ('96)
also obtained whole larvæ from one-half and one-fourth blastomeres,
and I also found that the one-eighth blastomeres do not develop
beyond the blastula stage. The number of cells of which the one-
half larva is composed is half that of the normal larva, and the one-
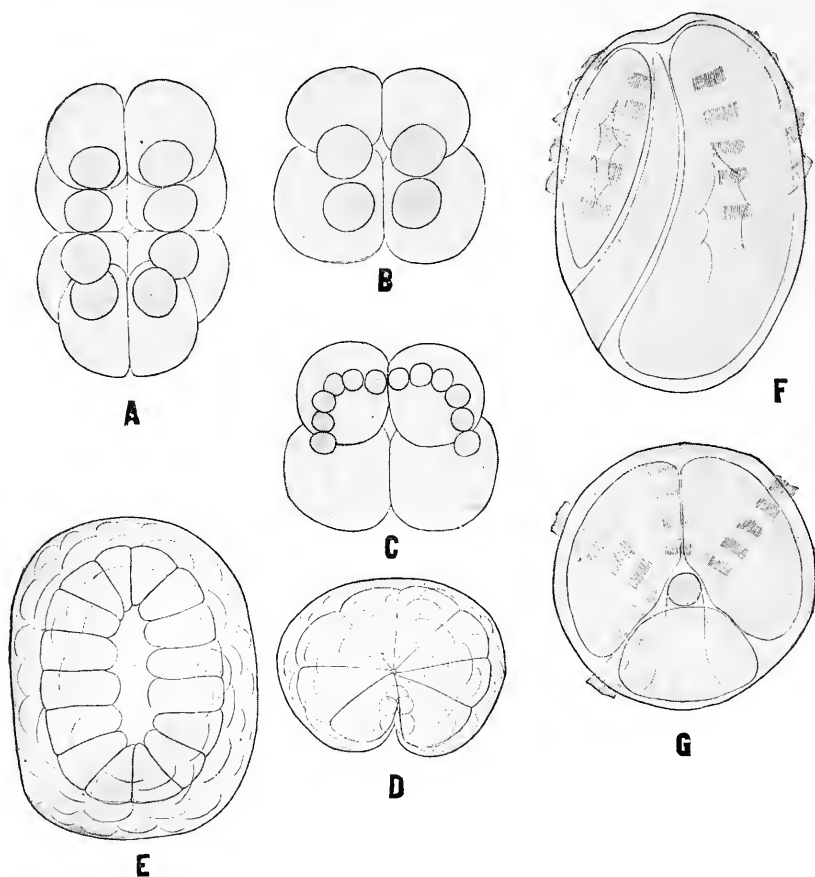


FIG. 66. — Ctenophore-egg and embryo. *A*. Normal sixteen-cell stage. *B*. Half-sixteen-cell
stage. *C*. Later half-segmentation stage. *D*. Later half-embryo. *E*. Corresponding whole
embryo. *F*. Half-embryo seen from side. *G*. Same seen from apical end. In *F* and *G*,
four rows of paddles present, three endodermal sacs and ectodermal stomach.

fourth larva is made up of one-fourth of the total number of cells.
    In all the preceding cases in which the blastomeres have been *sepa-
rated*, a whole embryo has developed, although the cleavage was
often like that of a part. In one form, however, it has been found
that a whole embryo does not develop. Chun ('92) first showed that
the isolated one-half blastomere of the ctenophore egg produced a

half-larva. He also inferred from certain incomplete embryos caught in the sea, that these incomplete larvæ could subsequently regenerate the missing parts. Driesch and Morgan ('95) studied the development of the isolated blastomeres of another ctenophore, *Beroë ovata*. They found that the isolated one-half blastomere divides exactly as a half of the whole egg (Fig. 66, *A*, *B*, *C*). It remains more or less a half-structure, even after the ectoderm has grown over the whole surface (Fig. 66, *D*). The invagination of ectoderm, to form the so-called stomach, that takes place at the lower pole of the whole embryo, is formed at one side of the lower pole in the half-embryo (Fig. 66, *F*, *G*). It pushes into the endodermal yolk mass, and lies not in the middle, but somewhat to one side. In the normal embryo there are formed four endodermal sacs or pouches in the central yolk mass that become connected with the inner end of the ectodermal stomach, around which they lie symmetrically. In the half-embryo two sacs are formed, and in addition a smaller third sac, which always lies on the side of the stomach that is nearest the outer wall (Fig. 66, *F*, *G*). The embryo is, therefore, somewhat more than half the normal embryo in regard to the number of its endodermal sacs.

There are present eight meridional rows of paddles in the normal embryos of the ctenophore. They lie symmetrically on the sides, converging towards an apical sense organ. In the one-half larva there are always only four of these rows of paddles that are not equally distributed over the surface, since on one side there is a wider gap between two of the rows than elsewhere (Fig. 66, *G*). The sense plate also lies somewhat eccentrically, *i.e.* more towards the side corresponding to that at which the other blastomere lay.

If the one-fourth blastomeres are separated, each continues to segment as though still a part of the whole. A one-fourth embryo develops that has an unsymmetrical stomach, with *two* endodermal sacs. There are only two rows of paddles. The embryos are, therefore, in several respects one-fourth embryos, but the presence of two endodermal sacs, instead of only one, shows that in this particular, at least, the embryo is more than a fourth of the whole.

The part of the work of Driesch and Morgan, that has a special bearing on the *interpretation* of the one-half and one-fourth development of the isolated blastomeres, is that in which some experiments are described which consisted in cutting off portions of the unsegmented egg. If a fertilized but unsegmented egg is cut in two by means of a small pair of scissors, the part that contains the nucleus may segment, and give rise to an embryo. The division is generally like that of a part, and in such cases an incomplete embryo develops. The embryo may have fewer rows of swim-plates than has the normal embryo, and fewer endodermal sacs, and the stomach may be in an

eccentric position. The embryos resemble in every respect the incomplete embryos from isolated blastomeres. It is important to note that although the embryos from isolated blastomeres resemble those from pieces of the segmented egg, in the former case the nucleus has divided once, and each blastomere contains half of the original nucleus, while in the latter case the entire segmentation nucleus is present in the piece. These facts seem to show that in this egg the incomplete development is directly connected with the protoplasm, and not with the nucleus, — a view that is maintained by Driesch and Morgan in connection with these experiments.

It was found in one or two instances that the nucleated pieces divided in the same way that the whole egg did, except that the blastomeres are proportionately smaller. From pieces of this kind whole embryos of small size developed. In this case we must suppose that the protoplasm has succeeded in rearranging itself into a new whole of smaller proportions.[1]

Crampton ('96) has shown in a mollusk, *Ilyanassa obsoleta*, that when a blastomere is separated from the rest, the cleavage proceeds as though the blastomere or its products were still present, and the larva is defective in those organs that are normally derived from that blastomere. These results are in line with those on the ctenophore egg. Fischel (1900) has also made some experiments on the segmented egg of the ctenophore, and has confirmed several of the results obtained by Driesch and Morgan. In addition he has tried the effect of disturbing the first-formed cells by pushing them over each other, so that their relative positions are changed. He finds as a result that the paddles, sense organ, etc., appear in unusual positions, and the latter may be doubled. This shows that we must regard the material or structural basis of the organs as present very early in the different parts of the egg, and that the organs develop without much regard to their relation to other organs.

Ziegler ('98) has also made some observations on the egg of this same ctenophore, that bear directly on some of the questions here raised. His study of the cleavage shows that the micromeres arise from the part of the egg that is opposite the pole at which the first cleavage furrow appears — the animal pole. Fischel's results have shown that the paddles and the sense organs arise from these micromeres, for, if the latter are displaced the former are also.

Ziegler performed the experiment of cutting off that part of an egg (which has just begun to divide) lying opposite the region in which the first furrow has appeared. In this way there was removed from the unsegmented egg the part from which the micromeres

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[1] We offered as a possible explanation in this case that the egg had been cut in two symmetrically with reference to the eccentric nucleus.

develop. Ziegler found that the micromeres still arise, and that from such pieces larvæ develop that have *eight* rows of paddles and *four* endodermal sacs. In one case two of the sacs were smaller than the others ; in another case one of the four was very much smaller than the rest. In another operation a large piece was cut from the egg, leaving a small nucleated piece that divided into two blastomeres of unequal size. An embryo developed from this small piece with four endodermal sacs, and only *four* well-developed rows of paddles. The four rows of paddles that were lacking were represented by two groups of a few plates each.

Ziegler gives a different interpretation of these results from that which Driesch and Morgan have offered. He interprets the last experiment, in which after the operation the piece divided into two unequal parts, and only four rows of paddles appeared, as meaning that the development of these organs on the smaller part is suppressed on account of the small size of the part. If the part had been still smaller all trace of the missing paddles might disappear, as he thinks was the case in certain experiments of Driesch and Morgan. There can be, I think, little doubt that if a piece is small enough, the result would follow as Ziegler supposes. It does not seem probable, however, that the pieces were really below the lower limit in the experiments of Driesch and Morgan, since the smaller blastomere was in one case as large as the whole piece (*i.e.* as both blastomeres taken together) in one of Ziegler's experiments.

Ziegler's results show very clearly that we are not obliged to think of the substance of the micromeres as laid down in the protoplasm of the egg, and hence there is no ground for supposing the substance of the paddles is *necessarily* present in the vegetative hemisphere of the egg. His results show that if the vegetative part is cut off, micromeres and paddles are still formed, although that part of the egg substance from which they normally arise has been removed. It should be pointed out, in this connection, that Driesch and Morgan did not suppose that the bases of the micromeres, or of the paddles, are actually laid down in a definite part of the protoplasm of the egg. They had also observed that in some cases whole embryos arose after a part of the egg had been removed, and this they attributed to the symmetrical position of the cut in relation to the organization of the egg. Ziegler's operations were made more or less in this symmetrical plane, excepting the one that gave rise to an incomplete embryo. Driesch and Morgan held that the formative factors become localized in the protoplasm, rather than arise from the nucleus, but pointed out that these observations do not lead to His's conclusion of localized germ areas in the egg.

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# CHAPTER XII

## THEORIES OF DEVELOPMENT

THE experimental work that Pflüger carried out in 1883 on the effect of gravity on the cleavage of the frog's egg, and the conclusions that he drew from his experiments, mark the starting-point for the modern study of experimental embryology.[1] We can trace the influence of Pflüger's results through most of the more recent work, and one of the conclusions reached by Pflüger, namely, that the material of the egg may be divided by the cleavage planes in any way whatsoever without thereby altering the position of the embryo on the egg, is, I think, one of the most important results that has yet been reached in connection with the experimental work on the egg. Pflüger's analysis of the factors that direct the development has also an important bearing on the interpretation of the development of a whole embryo from a part of an egg.

Pflüger found that in whatever position the frog's egg is turned before it begins to divide, the first two planes come in vertically, and the third horizontally, and that later the smallest cells are always formed in the upper hemisphere. He concluded, therefore, that gravity has some sort of influence in determining the position of the planes of cleavage. Pflüger observed that the position of the median plane of the body of embryos that have developed from eggs turned into unusual positions does not, as a rule, correspond to the plane of the first cleavage, but that the embryo generally lies on that meridian of the egg that passes through the primary egg axis and the highest point of the egg in its new position. Since any meridian may happen to be placed uppermost, the embryo may, therefore, develop upon any one of the primary meridians, and hence the material must be isotropous around the primary axis. Furthermore, since the embryo appears always below the middle of the egg, in whatever position the egg may lie, we must conclude that in each meridian the material is also isotropic.

It may be pointed out that while more recent work has substantiated, on the whole, the latter conclusions[2] of Pflüger, just stated, still

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[1] These experiments have been quite fully described in my book on *The Development of the Frog's Egg*.

[2] Not, however, the supposed action of gravity on the egg.

the results of studies of regenerative phenomena of organisms show that the conclusions are not necessarily the only ones deducible from the experiments; for, although it may be true that any possible primary meridian of the egg may become the median plane of the body of the embryo, it does not follow that there is no one organized plane always present in the normal egg, *i.e.* the egg may not be entirely isotropic. That this may be the case is shown in the regeneration of pieces of adult animals in which a piece cut to one side of the old median plane may develop a new plane of symmetry of its own. This possibility must be also admitted for the egg. If we substitute the term "totipotence," meaning that any meridian of the egg has the possibility of becoming the median plane of the embryo, in place of Pflüger's term "isotropy," we remove this element of possible error from his statement.

Roux and Born have shown that the only action that gravity has on the frog's egg is to bring about a rearrangement of the contents of the egg, a phenomenon that Pflüger had not observed. The lighter part flows to the highest region of the egg, and the heaviest to the bottom of the egg, hence the change in the position of the cleavage planes observed by Pflüger that begin in the upper, more protoplasmic part of the egg.

Another series of experiments, that we also owe, in the first place, to Pflüger ('84), consist in compressing the egg before and during its cleavage. The position of several of the cleavage planes may be altered, yet a normal embryo develops from the egg. The same experiment has been repeated by Hertwig ('93), and by Born ('93), on the frog's egg, and by Driesch ('92), Ziegler ('94), myself ('93), and others, on the egg of the sea-urchin, with substantially the same results. The value of the experiment lies not so much in showing that the coincidence between the first cleavage planes and the orienting planes of the body may be lost, as in showing that under these circumstances the nuclei have a different distribution in the protoplasm from that which they hold in the normal egg. Any theory of development that depends on the qualitative distribution of nuclear products during the cleavage period meets with great difficulties in the light of these results, and in order to overcome them will be obliged to add qualifications of such a kind as materially to alter its simplicity. Roux's theory, for instance, comes into this category. Roux ('83) suggested that since the complicated karyokinetic division of the nucleus is carried out in such a way as to insure a precise division of the chromatin, and since the qualities of the male are transmitted to the egg through the chromatin of the spermatozoon, it is probable that the division of the chromatin is a qualitative process, by means of which the elements are distributed to different parts of the egg.

According to Roux, the first division of the frog's egg divides the material of the right half of the embryo from that of the left; the second division separates the material of the anterior half from that of the posterior half. Roux limited, to a certain extent, his hypothesis to these two divisions of the frog's egg, and stated further that it is not improbable that during the later stages of development there may take place an interaction of the parts on each other, and this interaction would be another factor in the development. Weismann has adopted Roux's hypothesis, and has extended it to all organisms, and to most of the divisions of the developing egg, at least to all those divisions in which the qualities of the layers, tissues, organs, etc., are separated. On this slight basis he has constructed his theory of development and of regeneration It is important, therefore, to examine critically the evidence furnished by experimental embryology for or against this hypothesis of a qualitative division of the egg during the cleavage period.

The development of a half embryo from one of the first two blastomeres of the frog's egg, in Roux's experiment, seemed to support Roux's hypothesis, but it was not long before it was seen that the presence of the other blastomere vitiated the evidence to such an extent as to render it worthless, so far as this hypothesis is concerned. Then followed the experiments with the isolated blastomeres of the sea-urchin, amphioxus, jelly-fish, teleost, ascidian, triton, etc., in which each blastomere, when completely separated, gives rise to a whole embryo. From these experiments Driesch and Hertwig drew the opposite conclusion, namely, that during the cleavage there is a quantitative division of the egg into blastomeres that are equivalent, or at least totipotent. Roux attempted to meet the results of these experiments in two ways. He pointed out that in several of these cases the isolated blastomere divides as a half or as a fourth of the egg, and that in the sea-urchin this leads to the formation of an open half-blastula. In the second place, Roux brought more to the front his subsidiary hypothesis of the reserve germ plasm. He supposed that along with the early qualitative division of the nucleus, by means of which each part receives its particular chromatic substance, there is also a quantitative division of a sort of reserve germ plasm contained in the nucleus. Each cell *may* receive also a part of this material, and hence each cell may contain the potentialities of the whole egg. This reserve plasm may be awakened by any change that alters the normal development, as, for instance, when the blastomeres are separated. It may take some time for this reserve stuff to wake up, as shown by the half-development of the sea-urchin's egg that goes on for some time after the separation of the blastomeres. This hypothesis cannot be objected to on purely

formal grounds, but we are not so much concerned with a purely logical hypothesis as with a verifiable one.

It has been pointed out that the experiment of compressing the egg in different planes that leads to a new distribution of the nuclei is a formidable obstacle to Roux's hypothesis. If the nuclear divisions in the compressed egg are of the same sort as in the normal egg, we should expect to find as a result either a monstrous form with all its parts misplaced, or, if the parts are mutually dependent, nothing at all. Roux has attempted to meet this case by supposing that the nucleus itself responds to the change in the protoplasm and alters its divisions in such a way as to send to each part of the compressed egg the right sort of material for that part. This means that the nucleus can so entirely change the sequence of its divisions that instead, for instance, of sending to each pole of the first spindle the material of the right and left sides of the body, as it does normally, it may divide under compression in such a way that the material for the anterior half of the embryo is separated from that of the posterior half. That a change involving such a vast number of qualities could take place, as a result of the slight compression on the egg that brings about a change in the position of the spindle, seems highly improbable. It is, of course, not a disproof of the hypothesis to show that it involves very great complications, for the very assumption itself of a qualitative division of the nucleus, in the Roux-Weismann sense, involves us in great complications.

A more damaging criticism of the hypothesis of a qualitative division of the nucleus is found in an appeal to direct observation, which shows that the chromatin divides always into exactly equal parts. In many cases we know, from the subsequent fate of the cells, that two cells arising from the same cell play very different rôles in the subsequent development, yet the chromatin of the nucleus is always divided equally.

The development of the isolated blastomeres of the ctenophore egg may seem at first sight to give support to Roux's hypothesis, for in this case the first two cells are completely separated, and yet give rise to half-structures. Crampton's experiments on the eggs of ilyanassa may also appear to be evidence in favor of this view. In fact, however, they give no more support to the idea of a qualitative division of the nucleus than they do to that of a qualitative division in the protoplasm, and there are some further experiments on the ctenophore egg which indicate that it is the latter rather than the former sort of division that takes place. As stated in the preceding chapter, Driesch and Morgan found that, if a part of the protoplasm of the unsegmented egg of the ctenophore is removed, an incomplete embryo develops, although the whole of the segmentation nucleus is

present.   Ziegler's results show that, even after the removal of that part of the egg from which the micromeres develop, the segmentation may still be like that of the whole egg, and this shows that the egg has great powers of recuperation (at least in a symmetrical plane), so far as its protoplasm is concerned.   If, however, it is true that when a part is cut off unsymmetrically the protoplasm cannot reorganize itself, then the conclusion that Driesch and Morgan drew in regard to the protoplasm will hold, provided, as seems to be the case, the smaller blastomere of the first two is large enough to produce the typical structures.   The main point is this : If the protoplasm readjusts itself after the operation, so that the piece divides as a whole, a complete embryo develops ; if, however, the protoplasm does not readjust itself, and the piece divides as a part, an incomplete embryo is formed.   Since in both cases the same nucleus is present, and since the difference is obviously connected with a change in the protoplasm, it seems much more probable that the phenomenon of whole and half development is connected with the protoplasm and not with the nucleus.

The hypothesis that Pflüger, Hertwig, and Driesch have adopted, namely, that the cleavage divides the egg into potentially equal parts, stands in sharp contrast to the Roux-Weismann conception of development.   There are two ideas in the former view which should be kept, I think, clearly apart : the first is, that the blastomeres are potentially equal (isotropous), because they are exactly alike ; the second is, that despite the differences that may exist amongst them they are still potentially able to do the same thing, *i.e.* they are totipotent.   The former alternative is that adopted by Pflüger, Hertwig, and Driesch ; the latter view, to which Driesch seems more inclined in his later writings, is the one that I should prefer.[1]   The first four blastomeres of the sea-urchin's egg appear to be exactly alike, and we find that each can make a whole embryo.   If we assume, however, that despite their likeness and their totipotence they are different in so far as there is present in the protoplasm a bilateral structure, we are nearer, in my opinion, to the truth ; for, unless we assume the bilateral structure to be determined later by some external factor, of which there is no evidence, we must suppose that after fertilization, at least, there must be a bilateral structure to the protoplasm, and this view is borne out in one sense by the subsequent mode of cleavage of the blastomeres if they are separated.   Whether this bilaterality of the fertilized egg leads to the bilaterality of the cleavage is, however, a different question.   In some cases this *appears* to be the case, in others it is clearly not the case, and we must suppose that some other condition determines the bilaterality

[1] As stated in my article on " The Problem of Development," 1900.

of the later stages than that which influences the cleavage. Many facts of experimental embryology and of regeneration show, moreover, that a new bilateral structure may be readily assumed by pieces that have lost their connection with the rest of the organism.

After the third division of the egg of the sea-urchin, four of the blastomeres are somewhat different, so far at least as the material of which they are made up is concerned, from the other four; yet any one of the eight blastomeres, or groups of blastomeres, can produce a whole embryo. The same statement can be made for much later stages, since it has been found that fragments from any part of the blastula wall can give rise to whole embryos, and we may safely attribute this property to all the cells, although on account of the size of the cells of later stages they cannot individually produce a whole embryo, but each can produce any part of an embryo, which amounts to the same thing. If we assume that all of these cells are exactly alike, as Hertwig has done, we fail to see how the next stage in the development could take place, unless some external factor could act in such a way as to change the different parts of the egg. We have, however, no reason to suppose that all the cells are alike because they are all potentially equal. Even pieces of an adult animal — of hydra or of stentor, for example — can produce new whole organisms, although we must suppose these pieces to be at first as unlike as are the parts of the body from which they arise. Moreover, we do not know of a single egg or embryo in which we cannot readily detect differences in different parts of the protoplasm.

Can these gross differences, that we can see, in the materials of the egg explain the different development of the parts of the egg? It be shown, I think, that they do not *necessarily* determine the result. If we cut in two a blastula, so that one piece contains only the cells from the animal half and the other piece cells from the vegetative half, each produces a whole embryo; yet the one half lacked just those parts which by hypothesis were supposed to determine the gastrulation of the other half. If we suppose that the materials or structures that are characteristic of the vegetative half are gradually distributed from the vegetative to the animal pole in decreasing amounts, then any piece of the egg will contain more of these things at one pole than at the other. If, then, it could be shown that the gastrulation depends on the relative amounts of these materials in the different parts of the blastula, the difficulty met with in the former view disappears in part. I say in part, because the relative amount of materials that produces the results implies a connecting substratum that is acted upon and determines the result. Even if we suppose that this polar distribution of material could account for the polar invagination, we should still be at a loss to account for

the origin of the bilateral symmetry. In many eggs there is no evidence of a bilateral distribution of the material, although in some few cases there may be, so far as the form is concerned, a plane of bilateral symmetry. But even if it is supposed to be present in all eggs, and to coincide with the first plane of cleavage (or with any other cleavage plane), we still could not explain the bilateral symmetry of the one-half and one-fourth whole embryos that come from the corresponding isolated blastomeres. If a preëxisting bilateral plane exists in the egg, it must be reëstablished in some way in the isolated blastomere and in pieces of the blastula wall. In the latter case this could scarcely be brought about by a redistribution of the gross contents of the piece, since the presence of cell walls would interfere with such a process.

This analysis shows, I think, that the transformation of a piece into a new whole really involves a change in the fundamental structure itself. There cannot be much doubt that both the polarity and the bilaterality of the egg, or of a piece of the egg, belong fundamentally to the same class of phenomena, and we are forced to the supposition that they are inherent peculiarities of the living substance. Driesch thought at one time that it is only necessary to suppose that the protoplasm, and every part of it, possesses a primary polarity, and that some inequality in the material might determine the plane of bilaterality; but later he thought it necessary to assume also the presence of a bilateral structure in the protoplasm, and in all parts of it. This assumption of every part having a polar and a bilateral structure, and the polarity and bilaterality of the whole being the sum total of those of all its parts, is, I think, insufficient to meet the situation. If, for example, the first plane of cleavage coincides with the median plane of the body, the right blastomere has a structure that leads to the formation of the right side of the body, and similarly for the left blastomere. If the two blastomeres are separated, and each gives rise to a whole embryo with a new plane of bilateral symmetry, we must suppose that a new bilaterality has been produced. It does not make the problem any simpler to assume, as Driesch has done, that this is brought about by the elements rearranging themselves bilaterally on each side of a new plane that passes through the middle of the isolated blastomere, for what we need to have explained is what determines the new median plane. It seems to me that the problem is not any simpler, if we assume the polarity and bilaterality to be the property of a large number of elements, as Driesch has done, than if we assume at once the polarity and bilaterality as characteristic of the whole egg. The difficulty of understanding how a new bilaterality can be induced in a piece of the whole is as great on the one assumption as on the other. Not only

is it, I think, a much simpler idea to suppose the structure is something pertaining to the whole and is not the sum total of smaller wholes, but the idea is more in accord with other phenomena.

We meet here, I think, with precisely the same problem that we meet with in the regeneration of parts of adult animals. If a planarian is cut in two lengthwise, along the middle line, each half produces new tissue at the cut-side, out of which the missing half is formed. In this case the old median plane remains, more or less, as the median plane of the new worm, *i.e.* the structure of the new part is built up on that of the old. Very much the same result follows when the worm is cut longitudinally into two unequal parts. The larger piece retains its old plane of symmetry and adds to the cut-edge a new part that completes the symmetry. The smaller piece also builds up new material along the cut-edge, and a new plane of symmetry is formed between the old and the new parts. Here, also, a median plane is established at the edge of the old material, but in this case the material lay to one side of the old middle line, and this involves the changing over to a large extent' of the old material, so that it fits in with the new structures of the new median plane.

In those forms in which the readjustment takes place entirely in the old part, the change of conditions is more difficult to interpret. In some respects hydra gives us an intermediate condition, but since it is a radially symmetrical instead of bilaterally symmetrical form, the transformation is not so obvious. If a cylindrical piece is cut from the body, and is then cut lengthwise into two half-cylinders, each closes in and makes a cylinder of smaller diameter. A little new tissue may appear along the fused edges, but the missing half is not replaced, and a new hydra with a body of half size is formed from the piece. It is to all appearances a radially symmetrical form, and we must think, in this case, of the new axis of symmetry as having shifted to the middle of the piece. As yet no similar experiments have been made on a bilateral animal that regenerates by morphallaxis, so that we have nothing to appeal to for comparison with the bilateral egg, but the results, just described for the planarian and for hydra, indicate how a change might take place in pieces of adult animals that would lead to the formation in them of a new symmetrical structure. If we imagine a case of this sort, and suppose that after separating a piece from the side the cut-edge closed in and the piece assumed a symmetrical form, it is conceivable that a new plane of bilateral symmetry might soon appear in the middle of the piece owing to the symmetrical form of the piece; or the new plane of symmetry might slowly shift from the cut-edge toward the middle of the piece, after reaching which the balance or equilibrium would be attained. This statement, it must be confessed, is little more than a supposition, and rests on the unproven

assumption that the internal symmetry may develop in response to a symmetrical change in shape of the piece as a whole, which is partly the outcome of purely physical factors. At present, however, I see no other probable inference from the facts.

If we suppose a bilateral structure is present in the fertilized egg, and that it corresponds to the first plane of cleavage, a change of the sort that we have just sketched above may be supposed to take place when the blastomeres are separated. The stimulus is found in the new spherical form assumed by the isolated blastomere, and we may imagine the change to take place, in the way indicated, by virtue of the old bilaterality that is present, the change beginning at the side originally in contact with the other half.

There are several facts which seem to indicate that a change in the axial relations of the egg is very easily brought about before any definite organs have appeared. The fact that the point of entrance of the spermatozoon in the egg of the frog [1] and of the sea-urchin [2] may determine the first plane of cleavage points to this conclusion. The fact that, in the frog, and also in the triton, the median plane of the embryo corresponds sometimes to the first, sometimes to the second plane of cleavage, and sometimes to neither one, shows that the bilaterality of the embryo-structure may or may not coincide with the plane of cleavage. In the fish also there seems to be no corre-spondence between the planes of cleavage and those of the embryo, so that different factors may determine the two. We should not be justified in concluding from this evidence that a bilateral structure is absent, but rather that it is of such a sort as to be independent of the cleavage, and that it can be also easily changed. It is prob-able that the kind of organization that we must suppose to exist in the egg is of a very simple sort, and capable of easy readjustment. There is certainly no evidence in favor of the view that the organization of the egg need be anything like the organization of the embryo that comes from the egg, although the organization of the egg may be perfectly definite in its character. Until we know more of the nature of this organization, it is useless to speculate further as to how it can be altered.

Another question of much importance in connection with our present topic is the part played by the individual cells in the early development of the whole egg, or of any part of the egg. Hertwig ('93) thinks that the development is brought about by the action of the individual cells on each other. Driesch, when he states that the fate of a blastomere is a function of its position in the whole, does not commit himself definitely one way or the other so far as the cell as a unit is concerned. Whitman and others have urged the

[1] According to Roux.          [2] According to E. B. Wilson.

insufficiency of the cell theory, and think that cell boundaries play no important part in the development, but that the embryo develops as a whole. This has seemed to me to be the more probable view in the light of certain results of experimental embryology. Driesch, in later papers, has also opposed Hertwig's idea, and Wilson in his book on *The Cell* has also, to a certain extent, adopted this point of view. The formation of a typical larva in the sea-urchin and in amphioxus out of one-half or one-fourth the whole number of cells demonstrates, I think, the insufficiency of the cell-unit hypothesis. The discovery of continuous protoplasmic connections between neighboring cells, and the formation of new protoplasmic connections between all regions, as found by Mrs. G. F. Andrews,[1] gives us a basis of fact on which to rest the hypothesis of the embryo being a whole structure. This view meets with no great difficulty on the grounds that the nuclei are distinct centres of metabolic activity, for we know at present so little of what sort of action takes place between the nucleus and the protoplasm that we cannot rest our argument on any demonstrable relation.

The discovery that pieces below a certain minimum size are incapable of producing a whole organism is of capital importance. It has been pointed out that pieces of the egg of the sea-urchin less than one-sixteenth of the whole do not produce even the gastrula stage. In amphioxus the one-eighth blastomere seems to be near the lower limit of development. It has also been found that there is a lower limit for pieces of adult organisms below which they do not regenerate. This has been shown for hydra, tubularia, planarians, and stentor, and is probably true for all forms. This result is especially interesting in those cases in which the parts contain all the elements necessary to produce a new organism, and come from parts of the body that are totipotent in these respects. It seems certain that the lack of power of development in these cases is due entirely to the smallness of the piece. We can express the idea in another way by stating that a certain volume is necessary in order that a piece may produce the typical organization. This conclusion is important as showing that the organization is something enormously large as compared with the size of the chemical or physical molecules, and even of the crystal molecule. The size of a piece that is at the lower limit of organization is also very much larger than the smallest cells of which the embryo is made up, and this relation is a point in favor of the view that the organization is not simply the resultant of the interaction of the cells, but is something much larger than these cells; and we may even go further, I think, and add that it dominates the cells rather than is controlled by them.

[1] 1897.

In the light of the questions discussed in the preceding pages, we may now attempt to follow out in a more connected way some of the modern views and hypotheses dealing with the problem of development.

Hertwig, as we have seen, has opposed the Roux-Weismann hypothesis, and has formulated a view of his own. According to Hertwig, the cleavage divides the egg into equivalent parts, — an idea very similar to that of Pflüger. The cells he regards as units, and the development as the result of the interaction of the cells, — a process that in a way Roux had also assumed to take place between the different parts of the later embryo. Thus, while Hertwig's hypothesis contains little that is really new, it has selected portions from several already existing hypotheses, and united them into a consistent whole. It has been objected to Hertwig's view that the interaction of equivalent cells could never account for the introduction of new processes in the development; but if we grant that the cells are never entirely equivalent, whatever their potence may be, this objection can, I think, be met. Hertwig's chief service has been his destructive criticism of the Roux-Weismann idea of qualitative nuclear division.

Hertwig maintains that each stage in the development is the cause of the next stage, and states that a description of the series of stages through which the embryo passes gives a causal knowledge of the phenomena of development. He claims that beyond this descriptive knowledge we cannot hope to penetrate. Both Roux and Driesch have taken issue with Hertwig, and have pointed out that while each stage in the development contains within itself the causes of the succeeding stage, yet we gain no idea as to these causes from a simple description of two consecutive stages themselves. To state that the fertilized egg is the cause of the cleavage gives us no idea of what sort of a process the cleavage is, or how it arises, or what determines the sequence of the divisions, etc. The blastula, for instance, contains the factors that produce the gastrula; but to state that, in a physical sense, the blastula is the cause of the gastrula is an erroneous interpretation of what is meant by causal knowledge. If Hertwig's idea were correct, there would be as many causes in each embryo as there are stages in its development, and as many causes in the whole range of embryology as there are forms that develop multiplied by the number of stages in each embryo. What we should seek to discover is the particular cause that brings about each kind of process. If we could discover the cause in one single case, it is highly probable that it would be found to extend to a large number of other cases.

Driesch formulated an hypothesis of development in his *Analytische Theorie*, but has modified and changed it in several later contributions. It is difficult to give in a few words the subtile analysis

which Driesch has made of the phenomena of development. His ana-
lytical theory rests on the dictum that the prospective value of each
blastomere is a function of its position in the whole. By "function" is
meant "a relation of dependence of a general unknown kind." This
idea is connected with the following one, viz. that any blastomere
could be interchanged with any other one without altering the end-
result. A few elementary processes are supposed to be "given" in
the structure, or in the composition of the egg. Each elementary
process is the outcome of a cause, and each elementary process must
release the succeeding causes, — *i.e.* if the organization of the phase
A is present, one of the causes of the next phase B is also then present.
The first elementary process is the cleavage, that is initiated ("aus-
gelöst") by the fertilization. After a fixed number of divisions has
taken place, the cleavage process comes to an end. It has led to the
production of a number of cells having similar nuclei but having a
different plasma structure, and the result is the blastula stage. Or-
gans whose formation starts from the blastula stage are called primary
organs; the archenteron, the mesenchyme, the ciliated band, and the
mouth of the sea-urchin embryo belong to this class. Secondary
organs are those that arise from the primary ones, as the cœlom sacs,
for instance, in the sea-urchin embryo. The primary organs are
started by the setting free ("Auslösung") of a new elementary process
in the blastula, and later the secondary organs are started by new ele-
mentary processes that arise in the gastrula, which cannot appear until
the gastrula stage itself is present as a starting-point. In other
words, the elementary processes that are "given" in the egg can
only come into action, or be set free after a certain stage has come
into existence. This means that we must think of each organ that
responds to a stimulus as having the possibility of receiving that stimu-
lus, and also of answering to it. Even in inorganic nature every reac-
tion must depend on a specific receptiveness and a specific answer.
Driesch supposes that the receptivity is in the protoplasm, and the
power to respond is in the nucleus of each cell. In this way he
attempts to meet the difficulty that the nucleus is, in every cell, the
bearer of the totality of all the "Anlagen"; but inasmuch as it is sur-
rounded by a specific plasma, it is in a position to receive only cer-
tain stimuli, and can therefore only respond to certain causes.

In the specific nature of the cytoplasm of the cell lies the pro-
spective potence of every organ, and the possibilities of each cell are
limited by its plasma; the cell becomes more and more limited as
development proceeds. It may be said, therefore, that in the course
of development the cells become actually limited in their possibilities,
although they may still retain within themselves, in the nucleus, the
potentialities of the entire organism.

In the course of development each causal reaction brings about not only chemically specific differences, and thereby makes possible the introduction of new elementary processes, but the reaction also brings about by this very means a lessening of the possibilities of the cell, because each cell will now only respond to a more limited set of causes. We may say that the elementary process is not only the cause of the next change, but by virtue of its specific nature it is the beginning stage of the future reactions. Development proceeds from a few prearranged conditions, that are given in the structure of the egg, and these conditions, by reacting on each other, produce new conditions, and these may in turn react on the first ones, etc. With every effect there is at the same time a new cause, and the possibility of a new specific action, *i.e.* the development of a specific receiving station for stimuli. In this way there develops from the simple conditions existing in the egg the complicated form of the embryo.

In this brief summary of some of the essential features of Driesch's hypothesis, I have omitted some parts that seem to me to go beyond the legitimate field of a scientific hypothesis, — such, for instance, as the causal harmony of the reactions ; and other parts have been omitted because they are improbable in the light of more recent work. It would not be difficult to show that many difficulties beset each stage of the argument, or to show how slender a basis of fact there is to support some of the hypotheses. In fact, Driesch himself has modified very greatly some of the views of his *Analytische Theorie* in his later writings. The merits of the analysis should not be overlooked, however, since it is one of the first philosophical attempts to show how, in the light of recent discoveries, the process of epigenetic development may receive a causal interpretation. Even if the argument should break down, the hypothesis will remain an interesting contribution, opening the way to newer points of view in regard to the process of development. In later papers, especially in those dealing with the localization of morphogenetic processes, Driesch attempts to show that certain experimental results *demonstrate* that there is a vitalistic principle at work in the development of the organism from the egg, as well as in the process of regeneration. He bases his argument on the results of the experiment in which the gastrula of the sea-urchin egg is cut in two, as described already on page 234. The archenteron has not, at the time of the experiment, subdivided itself into its three characteristic parts. The posterior piece, that contains the posterior part of the archenteron (the anterior part having been removed with the anterior piece), produces a new whole embryo of smaller size, in which the archenteron is subdivided into three parts, that are in the same proportion to each other and to the whole embryo as are the same divisions of the normal archenteron. This proportionate formation of

the parts of the archenteron on a smaller scale cannot, Driesch claims, be accounted for on any known chemical or physical principle. There must be, therefore, a different sort of principle involved, and this Driesch calls the vitalistic principle.

It may be pointed out that this illustration that Driesch has selected is only an example of all proportionate development, which many observers have described as taking place in pieces of embryos. It is only a striking case of what has been also known in many cases of regeneration, of small pieces producing whole structures, and there is nothing new or startling in this demonstration of a vitalistic principle. The fact may be stated in another way, viz. that the proportionate development of an organ is, within certain limits, self-determining, or is self-determined by its size. The vitalistic principle that Driesch sees demonstrated in these results is the now familiar process of a smaller piece producing the typical structure on a smaller scale; a phenomenon that a number of other writers had already called attention to as one of the most remarkable phenomena connected with the regeneration of pieces of an adult organism, or of an egg.

It is something of this same sort that the older zoologists must have had in mind when they spoke of "formative forces" as peculiar to living things. The use of the word "force" in this connection has often been objected to, and not without justification; since it seems to imply that the action is of the sort for which the physicist uses the word "force." The fundamental question turns upon whether the development of a specific form is the outcome of one or more "forces," or whether it is a phenomenon belonging to an entirely different category from anything known to the chemist and the physicist. If we state that it is the property of each kind of living substance to assume under certain conditions a more or less constant specific form, we only restate the result without referring the process to any better-known group of phenomena. If we attempt to go beyond this, and speculate as to the principles involved, we have very little to guide us. We can, however, state with some assurance that at present we cannot see how any known principles of chemistry or of physics can explain the development of a definite form by the organism or by a piece of the organism. Indeed, we may even go farther and claim that it appears to be a phenomenon entirely beyond the scope of legitimate explanation, just as are many physical and chemical phenomena themselves, even those of the simplest sort. To call this a vitalistic principle is, I think, misleading. We can do nothing more than claim to have discovered something that is present in living things which we cannot explain and perhaps cannot even hope to explain by known physical laws.

Wilson ('94) has also rejected Roux's hypothesis of qualitative nuclear division, and adopts the view of the totipotence of the early blastomeres. He has also advanced the view that there is during development a progressive differentiation of the cells. In a later contribution ('96), he accepts "the view of Hertwig and of Driesch that the various degrees of partial development beginning with the echinoderm egg and culminating in the gasteropod may be due to varying conditions of the egg cytoplasm in the different forms." Wilson points out that the series of forms represented at one end by amphioxus and at the other end by the ctenophore and the gasteropod may be brought under a common point of view, "for it is certain that development must be fundamentally of the same nature throughout the series, and the differences must be of secondary moment."

If we reject, as several students of experimental embryology and of regeneration have done, the Roux-Weismann idea of the existence of pre-formed germs in the nucleus, and also the idea of Hertwig of the equivalency of the first-formed blastomeres, and Driesch's vitalistic principle, what position can we take in regard to the problem of development? We may at least attempt to formulate our present position.

There must be assumed to exist in the egg an organization of such a kind that it can be divided and subdivided during the cleavage without thereby losing its primary character. The refusion of the cells after each division by means of protoplasmic connections indicates how this may be possible. The organization must be thought to be of such a kind that the factors determining the cleavage may be different from those that determine the median plane of the body. This is demonstrated by Pflüger's experiment in which the position of the cleavage planes is changed, but the embryo appears in relation to the primary meridians. The first-formed blastomeres, that result from the division of the egg, do not seem to be strictly equivalent, but they appear to be in most cases, at least, totipotent. The characteristics of each part of the protoplasm may be a factor in determining what sort of structure may come from that part of the egg, but back of this lies the fundamental character of the protoplasm itself, that determines what each part, in its relation to the whole, can do. The division of the nucleus appears to be in all cases an exact quantitative division, and there is some evidence to show that the early nuclei are all equivalent, — or at least totipotent. The division of the protoplasm is often into unlike parts, and the kind of cytoplasm contained in a part may or may not limit the potencies of each part.

One of the most important facts in connection with the organization is that a part, if separated from the rest, may become a new whole, and this appears to be a fundamental peculiarity of living

things. Analogies can be found, perhaps, in inorganic phenomena, as for instance a storm dividing into two or more parts and each developing a new storm centre of its own, or when a suspended drop is divided and each half becomes a new sphere ; but these comparisons lack some of the essential features of the organic phenomenon.

A progressive change takes place as development proceeds, so that a stage once passed through is not repeated if a part is separated from the rest, as illustrated by Driesch's experiments with the blastula and gastrula of the sea-urchin and starfish, and by the method of development of pieces of the adult, that do not pass through the embryonic stages. As the protoplasm changes new conditions may arise, either because the protoplasm in its new form can be acted upon by those internal or external conditions to which it did not respond at first, as Driesch has supposed, or, as I think equally probable, because the series of reactions that have begun with the first step in the development work themselves out in the same way that a chemical reaction once started may pass through a long series of stages depending upon the nature of the substance. The difference between these views lies in this, that the former supposes latent substances, or elementary processes or forces, whatever they may be called, to be present in the egg and to act when a medium that responds to them has come into existence; the other idea supposes that the whole process is started with the first change and once set going is of such a kind as to continue to an end through a regular series of stages. Both views are suppositions, and, it may be, reduce themselves ultimately to the same thing.

On any theory of development, the nucleus cannot be left out of account, since the evidence that we now possess shows that through the nucleus even the most trivial peculiarity of one parent, and probably of both, may be transmitted. This has led a number of zoologists to look upon the nucleus as a body containing specific elements corresponding to those of the individual from which the nucleus has come, but inheritance through the nucleus is no more a demonstration of the existence of pre-formed elements of the male than are the general facts of embryology a demonstration of pre-formation. All we can legitimately conclude is that the substance of the nucleus is of such a sort that it acts on the cytoplasm in a definite way, and determines, in part at least, its differentiation. There has been steadily accumulating evidence to show that during development there is an interchange of material between the nucleus and the protoplasm, and it is not going far afield to conclude that the character of both nucleus and protoplasm is altered by the interchange in material. If this is admitted it is no more remarkable that a hybrid is midway between its parents than that a parthenogenetic egg produces a form like that of the individual from which it has come.

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Several writers, as we have seen, have adopted the view that the nuclei are storehouses of the undifferentiated germ plasm, and retain everywhere the sum total of the "Anlagen" of the egg nucleus. I do not know of any evidence that demonstrates that the nucleus is less modified in these regards than is the rest of the cell. On the contrary it seems to me that a fair case might be established in favor of the view that the nucleus and the cytoplasm cannot be contrasted in this way, and that a change in the cytoplasm may also involve a change in the nucleus.

The phenomena of regeneration show over and over again that differentiated cells may change into structures entirely different from what they have been, as illustrated in the development of the lens from the edge of the iris, and in the production of a new hydra, or tubularian, from a piece of an old one. It is, I think, an arbitrary assumption to suppose that this is brought about by a reserve stuff in the nucleus, for the production of new eggs and spermatozoa in the animal, from cells that have themselves passed through most of the early embryonic changes and have been parts of embryonic organs, shows that although the protoplasm may change throughout these stages, it may still come back to the starting-point, and there is nothing to show that this return is brought about by the nucleus. I cannot but think that Driesch was prejudiced by current opinion, when he adopted the view, as one of the foundations of his analytical theory, that the nucleus contains all the "Anlagen" of the whole organism, and that the protoplasm alone undergoes a progressive change.

The central problem for embryology is the determination of what is the cause or causes of differentiation. Our analysis leads us to answer that it is the outcome of the organization; but what is the organization? This it must be admitted is a question that we cannot answer. Looked at in this way the problem of development seems an insoluble riddle; but this may be because we have asked a question that we have no right to expect to be answered. If the physicist were asked what is gravity he could give no answer, but nevertheless one of the greatest discoveries of physics is the law of gravitation. If we could answer the question of what the organization is to which we attribute the fundamental phenomenon of development, there would perhaps be nothing further left to find out in the development of animals. Fortunately there is a different and safer point of view. There are other questions to which we can expect an answer. Because the physicist cannot tell what gravity is, he neither rejects the term nor despairs of obtaining a knowledge of how it acts. If our analysis of the problem of development leads us to the idea of an organization existing in the egg, our next problem is to discover how it acts during development. Most of the results described in several

of the preceding chapters have taught us something of how the organization behaves. We have found that it can be affected by external circumstances, even to such an extent that its polarity may be reversed. We have seen that if an organized structure is broken up into pieces, each piece may reorganize itself into a new whole. The most familiar, and at the same time the most difficult thing to understand, is that the organization is of such a kind that it has the property of passing through a definite series of stages leading to a typical result, and having reached its goal of throwing off organized bodies, or germ cells, that begin once more at the starting-point and pass through the same cycle. The action of the organism is sometimes compared to that of a machine, but we do not know of any machine that has the property of reproducing itself by means of parts thrown off from itself.

These are some of the most characteristic phenomena exhibited by the organization. In the final chapter some of the questions that have been suggested in connection with the method of action of the organization will be further discussed.

# CHAPTER XIII

## THEORIES OF REGENERATION

IT is significant to find that the theory of pre-formation of the embryo in the egg, that was so very widely held during the seventeenth and eighteenth centuries, and during the first part of the nineteenth century, was at once applied to the explanation of the regeneration of animals when this process became known. Bonnet in 1745 attempted to explain the newly discovered facts in regard to the regeneration of animals by means of the pre-formation theory. Just as the egg was supposed to enclose a pre-formed germ, so he imagined there lay concealed latent germs in the adult animal. At first Bonnet thought that these germs must be whole germs, like those contained in the germ cells of the reproductive organs, and that only as much of any one developed as was needed to replace the missing part. Later, however, he admitted that the germs might be incomplete germs, which are so located in each region that they represent the parts of the body beyond that region. The *purpose* of these germs is to replace any accidental injuries to the animal. He pointed out that some animals are more subject to injuries than others, and these animals are he thought especially well supplied with germs. Since in some animals the same part may be replaced several times, Bonnet assumed that on each occasion a new germ is awakened. As many sets of germs are present in these animals as the number of times the animal is liable to be injured in the course of its natural life.

Bonnet found that in lumbriculus a new head and a new tail may appear at almost any level, if the worm is cut in two, and, therefore, he supposed, head germs and tail germs are present throughout the worm. But why, if this is so, should a head germ always develop at the anterior end, and a tail germ at the posterior end of a piece cut from the body? Bonnet's keen mind saw that it was necessary to make a further assumption. He supposed that the fluids of the body that pass forward carry nourishing substances for the head. When the worm is cut in two these substances are stopped at the anterior cut-surface, and there accumulating act on the latent head germ, and nourishing it, cause it to develop. Correspondingly the nourishing

substances for the tail flow backward, and accumulating at the posterior cut-surface awaken a tail germ to activity.

The part of the body in which these nourishing substances are supposed to be produced is not specifically stated, but in one passage Bonnet says that the fluids that flow toward the head are there used up in that organ, and we may infer that he held a similar view for the posterior region. He offers no explanation of the cause of the flow of these substances in a given direction, and in this respect his hypothesis lacks support where it is most needed. In fact, it is no more improbable that a head germ should always develop at the anterior end and a tail germ at the posterior end, than that head-forming substances should flow in one direction and tail-forming in another. It is not that it is worth while to object to Bonnet's hypothesis on the ground that it does not explain everything, but it is worth while to point out that it gives only the appearance of an explanation, and that it begs the whole question by the assumption of particular nourishing fluids flowing in definite directions. So far as the blood is concerned, we know that the different parts of the body take from it those substances or fluids that they make use of, not that special fluids flow to particular regions. It is probable that Bonnet thought of the blood rather than of any other subtler fluids passing through the tissues; and, if so, there is nothing that we know in regard to the behavior of the blood that lends support to Bonnet's idea.

Bonnet takes care to state that the pre-formed germs may not appear to us like miniature copies of the part into which they develop, but they are so constructed that, as they absorb nourishment and become larger, they assume a characteristic form.

Weismann, who has also accepted the pre-formation hypothesis to account for the development of the egg, has applied the same conception of pre-formation to the process of regeneration. He believes that partial, latent germs are present in different parts of the body, and that these germs are present especially in animals that are liable to injury and in those parts of the body that are likely to meet with accidents. In these essential respects, Weismann's idea is the same as Bonnet's; but in regard to the location of the germs, and their manner of awakening, and as to how the forms, liable to injury, have acquired their power to regenerate, Weismann adopts more modern standards. He believes that the germs are located in the nucleus. Those that bring about the development of the egg are supposed to be different from those that bring about regeneration, because the method of regeneration is generally different from the method of development of the egg.

Regeneration, on Weismann's view, is brought about by latent cells containing pre-formed germs in the chromosomes of the nucleus.

These germs are called the determinants. Since at each level in an animal, or in a part of an animal, regeneration may occur and replace the missing part, it is assumed that the germs are correspondingly different at each level, and represent all the parts that lie distal to that region. Weismann does not suppose that there is a single germ at each level that represents all the distal parts, but that in each layer, or organ, or part there are many cells that contain germs corresponding to the distal regions. The qualities of the latent cells are sorted out by means of the qualitative divisions of the chromatic material of the nucleus. Moreover, since the new part can itself regenerate, the further assumption is made that during regeneration new subsidiary or latent cells are laid down at each level. This is supposed to be brought about by a quantitative division of each germ after it has reached its definitive position in the new part.

Weismann's general attitude toward the problem of regeneration is summed up in the following statements: " It may, I believe, be deduced with certainty from those phenomena of regeneration with which we are acquainted, that *the capacity for regeneration is not a primary quality of the organism, but that it is a phenomenon of adaptation.*" Again, " Hence there is no such thing as a general power of regeneration; in each kind of animal this power is graduated according to the need of regeneration in the part under consideration." " We are, therefore, led to infer that the general capacity of all parts for regeneration may have been acquired by selection in the lower and simpler forms, and that it has slowly decreased in the course of phylogeny in correspondence with the increase in complexity of organization, but that it may, on the other hand, be increased by special selective processes in each stage of its degeneration in the case of certain parts which are physiologically important and at the same time frequently exposed to loss."

The evidence brought forward in the preceding pages leads, I think, to precisely the opposite conclusions, and, in certain cases at least, it has been shown that there can be no relation between the power of regeneration and the extent of exposure of a part to injury or to loss. It is unnecessary to enter here further into this question, since it has been discussed already in Chapter V.

Weismann's statement that the power of regeneration has decreased " in correspondence with the increase in the complexity of the part " cannot by any means be entirely accepted. If the complexity of a part is of such a kind that the part cannot sustain itself independently until regeneration has taken place, or if the exposed surface of the wound is such that it cannot be closed over, or if the new part cannot be properly nourished, or if the tissues have changed in such a way that their cells can no longer multiply, then the statement is, to

a certain extent, true. On the other hand, when we find that one of the most complicated organs of the body, the eye, can regenerate in the salamander, if only a piece of the optic cup is left attached to the nerve, we may well doubt if there is any such direct and general connection between regeneration and complexity as Weismann maintains.

Weismann's so-called "mechanism" of qualitative nuclear division is the basis of his conception of pre-formation. We are, I think, at present in a position to reject not only this conception, since it finds no support either in observation or experiment, but also his view that regeneration is brought about by latent cells; for it has been shown in a large number of cases that the new cells come directly from the old, differentiated ones. In a previous chapter it has been pointed out that Weismann's idea that regeneration has been acquired by a process of natural selection, and is under the influence of this supposed agent, is in direct contradiction to a number of known facts. Under these circumstances we are warranted, I think, in concluding that the entire Weismannian point of view is wrong.

The process of regeneration has been often compared to the process by which a broken crystal completes itself. Herbert Spencer, in particular, has elaborated this idea. In his book on the *Principles of Biology*, he says: "What must we say of the ability an organism has to recomplete itself when one of its parts is cut off? Is it of the same order as the ability of an injured crystal to recomplete itself? In either case new matter is so deposited as to restore the original outline. And if, in the case of a crystal, we say that the whole aggregate exerts over its parts a force which constrains the newly integrated molecules to take a certain definite form, we seem obliged, in the case of the organism, to assume an analogous force." Spencer has called attention to a superficial resemblance between the renewal of a part of a crystal and the regeneration of an animal, and without further inquiry into the profound differences between the processes, assumes that "analogous forces" are at work. Now that we know something more of both processes, we find so much that is totally different, that there remains no basis for Spencer's conclusion, namely, that analogous forces must be present. Furthermore, Spencer's statement that the whole crystal aggregate exerts over its parts a force of some kind is diametrically opposed to our idea as to the method of "growth" of a crystal in a saturated solution. The new material is added always at the surface of the crystal, and the growth of each point is self-determining. There is no central force that controls the deposition of new material in the different regions. Rauber's work on the so-called regeneration of the crystal has given us a clearer conception of how the process is brought about. He has shown that when a piece is broken from a crystal, and the crystal suspended in a saturated solu-

tion of the same substance, it becomes larger by the deposition of new material *over all its surfaces*. The addition of new material may be more rapid over the cut-surface than elsewhere, but it must not be supposed that the more rapid "growth" takes place in order to complete the form of the crystal, for the growth over the cut-surface follows precisely the same laws that regulate the "growth" over all the other surfaces, that is taking place at the same time. In this respect we find an essential difference between the regeneration of a crystal and that of an animal, since in the latter the growth takes place only over the cut-surface; and, in forms that regenerate by proliferation, at the expense of the old material, so that the old material is correspondingly diminished as the new part grows larger. Regeneration may even take place in an animal deprived of all food, and also in one that is starving to death and diminishing in size. In those forms that regenerate by a change in shape of the entire piece into that characteristic of the typical form, the process bears not even the remotest resemblance to the process in the crystal. It is so obvious from every point of view that the comparison is entirely a superficial one, that it seems useless to point out further differences between the two processes.

Pflüger ('83) has given, in brief outline, an hypothesis to account for the process of regeneration. He states that since there is always replaced exactly what is lost, the new part cannot arise from a preexisting whole germ. If, for instance, the leg of a salamander is cut off at any level, as much comes back as is removed. The assumption of a leg germ is insufficient to account for the fact that only as much comes back as is lost, and not always a whole leg. Pflüger, therefore, offers another hypothesis. He assumes that food material is taken up at the wounded surface and organized into the substance of the new part. The new material is laid down at the surface of the old material, and is then organized into the kind of tissue that lay just beyond that region in the whole limb. Upon this first layer a new layer is deposited that is organized into the next part of the limb, and so on, until the whole missing part is replaced. Pflüger does not give any idea of how the new material is deposited at the cut-surface, but from what we know of the histology of the process we must suppose, if we should adopt Pflüger's interpretation, that new cells are produced by the old ones, and that these new cells form the successive layers out of which the new limb is produced. Pflüger speaks of an arranging molecular force, which we can only suppose, in the light of what has just been said, to act from cell to cell through the continuous protoplasm. Pflüger also pointed out that in certain cases the organization can take place only in a certain direction, that is, in some forms regeneration can take place from one side of a cut-sur-

face, but not from the other. He interprets this as due to a polarization of the protoplasm, one surface having peculiarities that are absent in the other.

There are certain objections to Pflüger's hypothesis that suggest themselves. In the first place the new part does not, in many cases, replace all that has been removed, and hence it is difficult to see how the building up in the way Pflüger supposes, could take place. In these cases the new material forms only the distal end of the part removed, and the relation of the old to the new part is of secondary importance. Again, in cases of heteromorphosis, as when a tail develops on an anterior cut-surface of a piece of an earthworm, the result must be due to quite different factors from those suggested by Pflüger. The results are, in fact, the reverse of what the hypothesis demands. Furthermore, when the entire piece is transformed into a whole new organism, there is very little in the process to suggest a change like that postulated by Pflüger. On the other hand there cannot be much doubt that the old part may have some influence, and in certain cases a very important influence on the new part, but whether this is a purely molecular influence is open to doubt. In whatever way this influence may act, it is only one of a number of factors that take a share in the result. The amount of new material, that is formed before the organization of the new part begins, seems to be also a factor; and the one that determines how much of the missing part can be replaced, and this in turn seems to be connected with the lowest organization size that can be produced. The distal end of the new part forms always the distal end of the organ that is to be produced. If enough new material has developed (before the organization of the new part takes place) to produce all of the missing part, the latter is formed, but if the material is insufficient to produce the whole structure, then as much of the distal end as possible is formed. In some cases, as in the planarians, the missing intermediate regions may subsequently develop behind the distal part that is first produced.

Sachs has advocated a view which has many points of similarity to that of Bonnet, although, in reality, it is not a theory of pre-formation at all, but one of pure epigenesis. His idea rests on the view that the form of a plant, or of an animal, is the expression of the kind of material of which it is composed. Any change in its material leads to a corresponding change in the form of the new parts. Sachs holds that the idea of many morphologists, that there is for each organism a specific form that tends to express itself, and which controls the development of the organism, is a metaphysical idea that has no ground in science. For instance, Sachs thinks that the flower buds of a plant develop, not because of some innate, mystical force

that causes the plant to complete its typical form, but because some substance is made in the leaves which, being carried into the growing region, becomes there a part of the material of that region, and from this new material a flower is formed. Simple and clear as this hypothesis appears to be at first sight, it will be found on more careful examination that it fails to account for some of the most characteristic phenomena of development and of regeneration. It may be granted at the outset that the presence of certain substances may undoubtedly influence the kind of growth of a new part; but, on the other hand, one of the most characteristic things of the organism is that it asserts its specific nature within quite a wide range of change, and, on the whole, resists the influence of other kinds of substances than those connected with its ordinary life. While Sachs looked no farther than the material substratum, and supposed that any change in this altered the form, there is, at present, sufficient evidence to show that it is the *structure* of the material that determines the most important changes that take place in it. This means, if we attempt to divest the statement of its somewhat metaphysical appearance, that the material of the organism is not simply a mixture of different kinds of materials, but a special kind of substance that has a definite structure of its own. This structure may, of course, be changed, but only by the addition of materials that the structure can take up as a part of itself. If the material does not become a part of the structure or organization, it is without effect on the form.[1] My meaning can, perhaps, best be illustrated by the method of regeneration of the tail of the fish from an oblique cut-surface. The growth of the new part is not determined by the kind or by the amount of the new material that is brought to the growing part, for, if it were, the new part would grow at an equal rate at every point; but the growth of the new part is regulated by the form of the tail of each particular kind of fish. The structure of the new part controls the growth of the material of the new part, and not the reverse. The only interpretation that can be given to this result is, I believe, that the new material assumes a definite structure, or what we may call an organization, and the subsequent changes are controlled by the kind of structure that is present; and since this structure has, as a whole, a definite form, we can state that the form controls the material, although the substitution of the word "form" for that of "the structure of the new material" may give the statement an unfortunate, metaphysical appearance.

In order to explain the regeneration of a piece of a plant, Sachs supposes that two substances are produced by the plant,— one a stem- (or leaf-) forming substance and the other a root-forming substance.

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[1] Unless it produces a physical change in the structure.

If either of these substances combines with the protoplasm of any part, a stem or a root is produced from that part. When a piece of the stem is cut from a plant, these two substances accumulate, one at the distal end and the other at the proximal end of the piece, and their presence in these regions determines that new shoots develop at or near the apex, and new roots at the base. Sachs tried to show that the direction of the flow of these two substances is determined by the action of gravity, — the lighter substance flowing to the higher parts, and the heavier to the lower parts. We find here reproduced Bonnet's idea of specific substances flowing in definite directions; but Sachs goes farther, and gives an explanation of the cause of the different directions taken by the two kinds of substances, viz. that it is due to the action of gravity. Vöchting has shown, as we have seen, after a thorough examination of the method of development of pieces of plants, that Sachs's hypothesis fails to account for the results; and he shows also that an internal factor, which he calls the polarization, has the most important influence on the regeneration.

It is not difficult to show that there are many other cases to which the stuff hypothesis does not apply. If, as Bonnet attempted to show, the regeneration is due to different stuffs, there is no explanation to account for the flow in animals of head-forming stuffs forward and tail-forming stuffs backward. In animals that regenerate laterally as well as anteriorly and posteriorly, we should be obliged to assume side-forming stuffs as well as head-forming and tail-forming stuffs; and since the kind of structures that are produced at the side are different at each level, we should be obliged to assume that there are many kinds of lateral stuffs. If regeneration can take place in a dorsal and in a ventral direction, as, for example, when the dorsal and the anal fins of teleostean fishes regenerate, there must also be stuffs to account for their development. When regeneration takes place from an oblique surface, it must be supposed that two or more of these kinds of stuff are brought into action. The regeneration of just as much of the limb of the salamander as is cut off also offers difficulties for Sachs's view. If we assume a leg-forming substance, it fails to account for the difference in the result at each level. If we assume that different substances come into play according to the amount of the leg that has been cut off, the hypothesis becomes as complicated as the facts that it pretends to explain.

A special case, to which the stuff hypothesis has been applied by Loeb and by Driesch, is that of tubularia, although the latter writer has used the hypothesis only to a limited extent as involving quantitative rather than qualitative results. There is present in the hydranth and stem of tubularia a red pigment in the form of granules in the endodermal cells. There is more of the red pigment in the stem near

the hydranth than elsewhere. If a piece of the stem is cut off, it closes its cut-ends, and a circulation of fluid begins in the central cavity. In this fluid globules now appear that contain the red-pigment granules. The globules appear to be free endodermal cells, or parts of such, that have been set free in the central cavity. In the course of twenty-four hours the new hydranth begins to appear near one end of the stem, and in this region of the stem a much larger number of granules appear. A little later all the red granules disappear from the circulation.

Driesch has supposed that the red granules of the circulation become a part of the wall of the new hydranth. The disappearance of the red granules at this time from the circulation would seem to give color to this view. But, on the other hand, I have found evidence showing that this interpretation is incorrect. In the first place, the granules that disappear from the circulation can be found lying in a ball within the digestive tract of the newly formed hydranth; hence their disappearance can be accounted for, and we find that they are not, or at least in large part are not, absorbed into the forming hydranth.[1] In the second place, there is a great increase in the number of endodermal cells in the region in which the hydranth is about to appear, and the thickening that results takes place some time before the granules begin to disappear from the circulation. The new granules appear in the new endodermal cells, and are presumably formed by them. Again, the hydranth, that develops later at the distal end, appears when there are no granules in the circulating fluid, and yet the hydranth may contain as much red pigment as does the proximal one. Lastly, the development of very short pieces shows that at the time of the formation of the new hydranth there is an enormous increase in the number of red granules in the piece, for there are many more of them contained in the new hydranth than were present in the entire piece at the time of its removal.

Loeb has not referred to the red granules in the circulating fluid, but simply to the red pigment which is present in the walls of the piece. This is supposed to move forward into the hydranth region, and call forth the development of a new hydranth. A study of the number of the granules in the stem gives no support to this idea, and the method of formation of single and of double hydranths in short pieces shows that the increase in the number of granules in the hydranth-forming region is not due to migration, but to local formation.

That specific substances may have an influence on the growth of certain parts cannot be denied, but it appears that in general they play a very secondary rôle as compared with other factors that

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[1] Stevens ('01) has found that this ball of red pigment is ejected from the mouth of the new hydranth.

determine the form of the organism or the development of a part. Vöchting's beautiful experiments ('86) on tuberous plants show that the presence of an excessive amount of food substances in the plant, brought about by the artificial removal of the natural storehouses for such material, may act on certain parts, such as the axial buds, or on the stem, and cause them to produce structures that they do not produce under ordinary circumstances. The axial buds become swollen and produce tuber-like bodies above ground, especially if the parts are enclosed so as to be in the dark, since the light retards the growth of tubers of all sorts. But it should not be overlooked that these buds and stems are structurally the same things as the tuberiferous stolons that have been removed, and hence the excess of material is stored up in them in the same way as it is under normal circumstances in the underground stems or stolons. The reaction is one normal to the plant, although it usually takes place in a different part.

The preceding hypotheses that have been advanced to account for the phenomena of regeneration, draw attention to some of the most fundamental problems of regeneration and, even in those cases in which the hypotheses have not given a satisfactory solution of the problems, some of them have served the good purpose, both of directing attention to important questions and of leading biologists to make experiments to test the new points of view. We should not underrate their value, even if they have sometimes failed to give a solution of problems, for they have been useful if only in eliminating certain possibilities, and this simplifies all future work. So long as an hypothesis is of a sort that it is within the range of observational and experimental test, it may be of service, even if it prove erroneous; for our advance through the tangled thread of phenomena is not only assisted by advances in the right direction, but all possibilities must be tested before we can be certain that we have discovered the whole truth. The value of a scientific hypothesis depends, it seems to me, first, on the possibility of testing it by direct observation, or by experiment; second, on whether it leads to advance; and, lastly, on its elimination of certain possibilities.

The experiments described in Chapters II, III, IV, have shown that there are many resemblances between the phenomena of growth and of regeneration. It has been pointed out that when it could be shown that certain external agents have a determining influence upon growth, these same agents have a similar effect upon regeneration. This also holds apparently for internal factors, although it is much more difficult to demonstrate that this is true. The presence of an abundance of food material in the tissues hastens regeneration in the same way that growth is more rapid in a well-fed organism. Food may, however, be looked upon rather as an external factor than as an

internal one. An excellent example of an internal factor is found in the interrelations of the parts to each other. This is shown in the development of a piece of a plant in which the apical buds develop faster than the proximal ones, and it appears that, in some way, the development of the latter are held in check by the development of the apical ones. Another case is found in the development of the bilobed tail of certain fish in which particular regions are held in check, while others grow at the maximum rate.

It is a curious fact that while we can cite several kinds of external influences that affect the development and the regeneration of organisms, the only internal factors that have been discovered are the so-called polarity and this interrelation of the parts. Perhaps there should also be added the specific nature of certain parts, limiting the possibilities of new growth in these parts, and the presence of the nucleus as necessary for the growth and regeneration of the organism.

If it be admitted that the same factors that affect the growth also affect in the same way the regeneration, we have made a distinct advance. It is, moreover, not difficult for us to understand how this is possible. If we consider first those cases in which growth takes place at one or more points at which the cells are undifferentiated, and compare this condition with that in regenerating animals that produce new tissue by proliferation, we can picture to ourselves that the same factors would act on the undifferentiated tissue in the same way in both cases. This does not explain what causes the organism to produce the new cells that appear over an exposed surface, and we must search for other factors to account for the out-wandering of cells, and for the local multiplication of the cells at the cut-end. We find a parallel to those cases in which the growth of an organism takes place throughout the whole body, in those animals in which the regeneration also takes place in the old part. This comparison should not, however, be pushed too far, since, in some forms, as, for example, a salamander, the growth of the animal takes place throughout the body, while regeneration takes place by the proliferation of new material. The difference in the regenerative process in a salamander and in a form like hydra is not due so much to the inability of the old cells of the salamander to increase in number as compared with those of hydra, but rather, it appears, to a certain rigidity or stiffness of the body of the salamander that prevents the rearrangement of the parts ; and the recompletion of the form takes place in the direction of least resistance, *i.e.* at the open or cut-end of the body.

Regeneration by means of morphallaxis takes place only in those forms in which the body is not made up of a series of separated

parts. This kind of regeneration occurs in those organisms in which the normal growth consists only in the enlargement of a system of organs already present. A piece of an animal of this sort usually contains the elements of each kind of organ, and from these the new parts are produced, both by proliferation at the cut-ends and by the enlargement of the parts that are present in the piece. In forms with separate segments we find, in some cases, resemblances between normal growth and regeneration, as shown, for example, in the earthworm. There is present in the young worm a region in front of the last segment, or, rather, a part of this segment, from which new segments are formed. In the regeneration of the posterior end a knob of new tissue is formed, and out of this a few segments develop, the last one having a growing region similar to that in the young worm. The subsequent stages in the regeneration involve the formation of new segments from the last one, as in the young worm. There is no such growing zone at the anterior end of the young worm, and none is formed in the regeneration of an anterior end, so that only the segments that are first laid down in the new part are present in the new anterior end.

An interesting comparison may be made between the phenomenon of growth and that of contraction and expansion of the protoplasm. The bending of heliotropic organisms toward or away from the light, and the similar bending of negatively stereotropic forms away from contact with a solid body, are supposed to be phenomena of growth, and resemble in many ways the phenomenon of contraction. In a plant that bends toward the light, it is found that the most obvious change involves the amount of water on the two sides of the stem, and this is most probably connected with a fundamental structural change in the protoplasm, that is too subtle for further analysis. In the regeneration of some forms it is found that they respond in the same way to light. While it cannot be demonstrated that these phenomena really depend on processes of contraction and of expansion, the results are nevertheless suggestive from this point of view. Furthermore, I think, one cannot study the regeneration of such forms as planarians, hydras, stentors, etc., without being struck by the apparent resemblance of the change in form that they undergo to a process of expansion. The idea of the expansion of a viscid body carries with it, of course, the idea of tension within the parts, and the return to the former condition is brought about by a release from the tension and a return to a more stable condition. If by the intercalation of new material the extended condition is fixed, a new state of equilibrium will be established.

It has been already pointed out that in a piece of a plant suspended in a moist atmosphere, the apical buds are those that first develop,

and also grow faster than the others. The buds situated nearer the base may not even begin to develop, although they are at first as favorably situated, so far as external circumstances are concerned, as the uppermost ones. The roots appear first over the basal end, and those nearer the base grow faster than do those nearer the apex. There cannot be much doubt that the suppression of the basal buds and of the more apical roots is connected with the development of the apical buds and of the basal roots. This can be shown by cutting a piece in two, when some of the basal buds will grow into shoots and the apically situated root-buds, that are now on the base of one piece, will begin to grow. It seems to me this relation can be at least more fully grasped, if we look upon it as connected with some condition of tension in the living part. The tension can be thought of as existing throughout the softer, more plastic parts. As long as the apical bud is present at the end of a stem or branch, or even near the apex, it exerts on the parts lying proximal to it a pull, or tension, that holds the development of these parts in check ; but if the apical bud is removed the tension is relaxed, and the chance for another bud developing is given.

It may be asked, how can it be explained that only the more apically situated buds of a piece develop, rather than the basal ones, since with the removal of the piece from the plant the tension has been removed also. The only answer that can be made, so far as I can see, would be that from the apex of the plant to its base the tension is graded, being least at the apex and increasing as we pass to the base. Those buds will first develop that are in the region of least tension, and their development will hold in check the other buds by increasing or reëstablishing the tension on the lower parts of the piece. A new system is then established, like that in the normal plant.

There are certain experiments with hydra that can, perhaps, be brought under the same point of view. When two long posterior pieces are united by their anterior cut-surfaces, each piece regenerates a circle of tentacles near the region of union, and each may produce a new head ; or only one head, common to both pieces, develops at the side. Each piece has retained its individuality, which may be interpreted to mean that each piece has retained its original condition of tension. If, however, after a union of this kind one piece is cut off, as soon as the two have well united, near the place of union, so that it is relatively small as compared with the other component, it may produce a head at its exposed basal end, and neither heads nor tentacles may develop at the place of union of the pieces.

It is probable, in this case, that the larger component has acted on the smaller one, so that its polarity is changed and becomes like

that of the larger component. It is possible, I think, to interpret this result in terms of our tension hypothesis. The condition of tension in the larger piece has overcome that of the smaller piece, so that the latter comes to have the same orientation that the larger piece has ; and the development of a head at the free end then takes place. The development of this head holds in check the development of a head at the anterior end of the larger piece in the region of union of the pieces. When two pieces of hydra are united by unlike poles, *i.e.* so that they have the same orientation, it is found that if the pieces are not too long, a head develops at the free end and none in the region of grafting. The result is similar to that in plants ; the development of the head at the free end suppressing any tendency that may exist to produce a new head by the posterior piece at the place of union. If the pieces united in this way are very long, a head develops at the apical end, and, in some cases, also near the line of union. This may be due to the pieces being so different at the place of union, that a head develops below this region before the unification of the two pieces is brought about, or because the formation of the head at the free end is relatively so far removed from the place of union of the pieces, that it does not influence the development of a head in this region.

These cases of grafting also illustrate another point of some interest. They show that the development of a head at the anterior end of a piece is not the result of the injury from the cutting or due to the action of some external condition on the free end, for the regeneration may take place when two anterior ends have been perfectly united to each other. The result can only be explained as the outcome of some internal factor such as polarity.

These examples have been chosen from hydra rather than from tubularia, in which somewhat similar phenomena have been observed, because in hydra the development of heteromorphic structures is of rare occurrence, while in tubularia external influence often calls forth a heteromorphic development. There cannot be much doubt, however, that in tubularia the same kind of internal factors are also at work. ‘

A more striking illustration of the possible influence of tension of the parts is shown by an experiment with planarians. If the head of a planarian is cut off and the posterior piece is split partially in two along the middle line, as shown in Fig. 31, *A*, and then one of the halves is cut off just anterior to the end of the longitudinal cut, the result is as follows : A new head develops at the anterior end of the long half (Fig. 31, *B*), but no head develops on the posterior cut-surface, provided this part has reunited along the middle line with the long half, and a line of new tissue connects the anterior

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cut-surface of the long half and the more posterior cut-surface of the shorter half. At least this happens if the piece is not split too far posteriorly, *i.e.* through the region of the pharynx. If this is done, a new head may develop from the posterior cut-surface. In another way the development of the more posterior head can be brought about. If the shorter side-piece is kept from fusing with the longer side-piece in the middle line, it will invariably produce a new head (Fig. 31, *C*). The lack of development of the posterior head, when the two cross-cut surfaces are united by a connecting part of new material, can, it seems to me, be best explained by the influence of the developing anterior head, or of the new side on the posterior new tissue, and this influence can, I think, be better appreciated if we suppose some sort of tension to be the influence at work.

Another example may be cited that shows even more clearly that the internal factor regulating the growth in the new part is probably some sort of tension. I refer to the development of the tail of fundulus from an oblique cut, or of the bilobed tail of stenopus from a cross cut. The assumption of the typical form that leads to the holding in check of the growth in certain regions, as compared with others, can be best understood, I think, as due to some sort of tension established in the different parts, that regulates the growth in those regions.

It is evident that whatever factor will serve to explain the preceding cases must also be expected to apply to the development of the whole embryo from parts of the egg or blastula, if the position that I have taken is correct, namely, that these phenomena belong to the same general group. Does the tension hypothesis make clearer the development of a whole embryo from a part of an egg? This means, can we think of the readjustment that takes place as due to the establishment of a characteristic equilibrium that expresses itself in the tensions of the different regions? There is, so far as I can see, no difficulty in supposing that the organization is at bottom a system of this kind; indeed, it seems to me that from this point of view we can get a better appreciation of the organization and of the series of changes that take place in it during development. The example that Driesch has chosen as a typical one of vitalistic action, namely, the proportionate development of a part of the archenteron of the half-embryo, seems to me to be likewise a case to which we can apply the tension view.

In these, as well as in all other cases, we must think of the tensions as existing, not only in one direction, but in the three dimensions of space, and of all combinations of these. The material in which the tensions exist must be thought of as labile, so that a change in one region involves a rearrangement in many cases of the entire sys-

tem. The new rearrangement appears to take place on the foundations of the old system.

It may appear that this idea of a system of tensions is too vague, that it fails to point out how the reorganization takes place, and that it gives not much more than the facts do themselves. There is a certain amount of truth in these objections which I fully appreciate, but something further can be said on these points. The view is vague in so far as we cannot picture to ourselves in a mechanical way just how such a system could bring about the suppression of growth in one region and allow the maximum amount in another region. But this is asking too much, since the hypothesis can only claim, at present, to furnish a means by which we can at least imagine what sort of a process is involved, and cannot give the details of the process itself. It can be shown experimentally that if the phenomenon is one of tension certain results should follow that are observed to take place, as when by keeping the shorter half of the planarian from reuniting to the larger half, or by breaking the union if it has been formed, a head develops also at the posterior cross-cut. In the second place, although we cannot understand how the rearrangement of the tensions in a piece takes place, yet from a causal point of view we can see how a change in one region of a labile system may produce, by means of a change of tension, a complete rearrangement of the parts throughout. It can even be claimed for the tension hypothesis that it at least becomes easier for us to see how such a change could take place, because it represents the organization as the expression of a system under tension, and hence, if the material is sufficiently flexible, a readjustment will probably take place when the system is changed in any region. It enables us to see how the organization of the egg may be divided by every cell division, and yet after the reunion of the cells the original equilibrium be established. We may perhaps claim, therefore, that in these respects the hypothesis does give us something more than do the facts; and, inasmuch as it brings a large number of phenomena under a common point of view, the idea may be worth further consideration.

In conclusion, I may add that the hypothesis is, I hope, also a legitimate one, in the sense that being within reach of an experimental proof or disproof, it may serve at least as a working hypothesis. Perhaps more fundamental than the idea that a system of tensions exists throughout the organization is the conception that the organization is itself a system of interrelated parts, and not a homogeneous substance or a mass composed of a large number of repeated parts, or rather, despite the presence of smaller, repeated units, the organization is not the result of their interaction, but of their regular arrangement as parts of a whole structure. If, then, this inter-

relation of the different parts of the structure can be looked upon as the result of a system of tensions, we can at least form a better idea as to how a piece of a whole can readjust itself into a new whole of smaller size.    And it is this possibility of rearrangement or regulation that is one of the most characteristic properties of living things.

# CHAPTER XIV

## GENERAL CONSIDERATIONS AND CONCLUSIONS

In the preceding chapters certain matters had to be taken for granted, since it was not possible, or desirable, at the time to discuss more fully some of the terms that are in common use, or to analyze more completely many of the phenomena. It was also not necessary to give the general point of view under which the phenomena were considered in their physical, chemical, or even causal connection. Little harm has, I trust, been done by relegating such questions to the final chapter. An attempt will now be made to give more explicit statements in regard to the use and meaning of such terms as "organization," "polarity," "factors," "formative forces," "vitalistic" and "mechanical principles," "adaptation," etc.

It will be found that the hypotheses that have been advanced to account for the phenomena of development and of regeneration may be roughly classified under two heads : first, those in which the organization is "explained" as the result of the collective action of smaller units ; and second, those in which the organization is itself regarded as a single unit that controls the parts. Let us examine these points of view more in detail, in order to see what has been meant in each case by "the organization."

A favorite method of biological speculation in the last forty years has been to refer the properties of the organism to invisible units, and to explain the action of the organism as the resultant of their behavior. The hypothesis of atoms and of molecules, by means of which the chemist accounts for his reactions, has proved so exceedingly fruitful as a working hypothesis that it has had, I think, a profound influence on the mind of many biologists, who have, consciously or unconsciously, attempted to apply a similar conception to the structure of living organisms. The discovery that all of the higher organisms are made up of smaller units, the cells, and that the lower organisms are single, isolated cells, comparable to those that make up the higher forms, has also drawn attention to the idea that the whole organism is the result of the action of its units. Furthermore, within the cells themselves units of a lower order have also been discovered, such, for instance, as the chromosomes, the chloro-

phyl bodies, etc., that repeat on a smaller scale some of the fundamental properties of the entire organism, as growth and division. It has been assumed that still farther down in the structure there are smaller units having the same properties, and the smallest of these are the ultimate units. The organism is looked upon as the result of the properties of these minute germs. The gemmules of Darwin furnish an example of an hypothesis of this sort; also the intracellular pangens of De Vries, the plasomes of Wiesner, the biophors of Weismann, the idiosomes of Hertwig, and the micellæ of Nägeli are other examples of this way of interpreting the organization. These elements are endowed by their inventors with certain properties, and these are of such a sort that they give the appearance of an explanation to organic phenomena. It is useless to object to these hypotheses that they are purely ideal, or fictitious, and that those properties have been assigned to the germs that will bring about the desired explanation, and have not been shown to be the real properties of the germs themselves. But apart from the arbitrariness of the process, it cannot be claimed that a single one of these creations has been shown to be true, or has even been accepted by zoologists as probable. A more serious objection to this point of view is that the most fundamental characteristics of the organism, those that concern growth, development, regeneration, etc., seem to involve in many cases the organism as a whole. So many examples of this have been given in the preceding pages, that it is not necessary to go over the ground again. It has been shown that a change in one part takes place in relation to all other parts, and it is this interconnection of the parts that is one of the chief peculiarities of the organism. In phenomena of this kind even the cells seem to play a secondary part, and if so, we can, I think, safely leave out of account the smaller units of which the protoplasm is supposed to be built up and we can neglect them, if for no other reason than this, that the argument that has called them into existence starts out with the cell as the highest unit. If the cell can be thrown out, most probably the units of which the cell itself is supposed to be made up can be safely disregarded also.

It may be objected that only through a knowledge of the minute structure of the organism can we hope to understand the behavior of the whole; but my point of view is not that there may not be a fundamental structure, but that this is not formed by a repetition of elements, which give to the whole its fundamental properties. It can be shown, I think, with some probability that the forming organism is of such a kind that we can better understand its action when we consider it as a whole and not simply as the sum of a vast number of smaller elements. To draw again a rough parallel; just as the properties of sugar are peculiar to the molecule and cannot be ac-

counted for as the sum total of the properties of the atoms of carbon, hydrogen, and oxygen of which the molecule is made up, so the properties of the organism are connected with its whole organization and are not simply those of its individual cells, or lower units.

The strongest evidence in favor of this view is found in the behavior of small pieces of an egg, or of a protozoon, or even of a many-celled organism. A lower limit of organization is very soon reached, below which the piece fails to produce the characteristic form, although all the necessary elements are present in the piece to produce the entire structure. The size of these pieces is enormously large as compared with the size of the cell, or of the imaginary elements of Nägeli, Weismann, Wiesner, etc. These results indicate that the organization is a comparatively large structure.

A few writers have either ignored the presence of smaller units, or have dealt with the organism from a purely chemical and physical point of view. They attempt to account for the changes in the organism as the outcome of known physical and chemical principles. It must, of course, be granted that in a sense the properties of the organism are the result of the material basis of the organism; but in another sense this idea gives a false conception of the phenomena of life, because, if we were simply to bring together those substances that we suppose to be present in the organism we have no reason to think that they would form an organism, or show the characteristic reactions of living things. Even from a chemical point of view we can see how this result could not be expected, for it is well known that the order in which a compound is built up, *i.e.* the way in which the atoms or molecules are introduced into the structure, is an important factor in the making of the compound. When we remember the immense period of time during which the organisms living at present have been forming, we can appreciate how futile it will be to attempt to explain the behavior of the organism from the little we know in regard to its chemical composition. Its chief properties are the result of its peculiar structure, or the way in which its elements are grouped. This structure has resulted from the vast number of influences to which the organism has been subjected, and while it may be granted that if we could artificially reproduce these conditions an organism having all the properties that we associate with living things would result, yet the problem appears to be so vastly complicated that few workers would have the courage to attempt to accomplish the feat of making artificially such a structure. To prevent misunderstanding, it may be added that while from the point of view here taken, we cannot hope to explain the behavior of the organism as the resultant of the substances that we obtain from it by chemical analysis (because the organism is not simply

a mixture of these substances), yet we have no reason to suppose that the organism is anything more than the expression of its physical and chemical structure. The vital phenomena are different from the non-vital phenomena only in so far as the structure of the organism is different from the structure of any other group of substances.

Nägeli has stated that each part acts as though it *knew* what the other parts are doing. His idea of the idioplasm involves a conception of the organism as a whole and not simply the sum total of a number of parts. Hertwig, who maintained at one time that the development of the embryo is the resultant of the action of the cells on each other, admits in his work on *Die Zelle und die Gewebe* that while this is in part true, yet on the other hand the whole also exerts an influence on its parts. Driesch, who hypothetically suggested at one time that the nuclei act as centres of control of the cell by means of enzymes, has later adopted a widely different view. Whitman has made a strong argument to the effect that the cell theory is too narrow a standpoint from which to treat the organism, and on several occasions I have urged that the organism is not the sum total of the action and interaction of its cells, but has a structure of its own independent of that of the cells.

This discussion will suffice to show some of the opinions that have been held as to the nature of the organization of the organism. Let us next ask what properties we may ascribe to it.

It has been found that certain polar, or rather dimensional, relations are characteristic of the organization. The term "polarity" expresses this in a limited way, but refers only to one line having two directions, while we now know that the dimensional properties relate to the three dimensions of space, and for this idea we might make use of the term heterotropy. Thus we find that a piece of a bilateral animal regenerates a new anterior end from the part that lay nearer the anterior end of the original animal, a new right side from the part that was nearest the original right side, and a new dorsal part from the region that lay near the original dorsal part, etc.

The polarity of a part can be changed in certain forms, as in tubularia, by exposing the posterior cut-end to the external factors that bring about the formation of a hydranth, or, as in hydra, by grafting in a reversed direction a smaller piece on a larger one. In *Planaria lugubris* and in the earthworm the polarity of the new tissue may be reversed, as compared with that of the part from which it develops, if the new part arises from certain regions of the body. A curious instance of the effect of the polarity is shown by the regeneration from an oblique surface in planarians. The new head arises from the more anterior part of the new material, rather than from the

middle of the anterior oblique surface, and the new tail arises from the more posterior part of the posterior oblique surface.   As an analysis of this result has been already attempted in an earlier chapter, it will not be necessary to go further into this question here.

The development of a new part at right angles to an oblique surface has also been described, and it has been pointed out that the result appears to be due to the symmetrical development of the new structure in the new part.   This symmetry of the newly forming part must be also counted as one of the properties of the organization.

Finally, the mode of regeneration of a new, bifurcated tail in the teleost, stenopus, shows that the new part may very early become moulded into the characteristic form, and that the growth of the different parts is regulated by the structure assumed at an early stage.   The new part does not grow out at an equal rate until it reaches the level of the notch of the old tail, and then continue to grow at two points to produce the bilobed form of the tail; but the bilobed condition appears at the very beginning of the development.

These illustrations give us nearly all the data that we possess at present on which to build up a conception of the organization.   That we must fail in large part fully to grasp its meaning from these meagre facts is self-evident.   The main difficulty seems to lie in this, — that when we attempt to think out what the organization is we almost unavoidably think of it as a structure having the properties of a machine, and working in the way in which we are accustomed to think of machines as working.   The most careful analysis of the "machine theory," as applied to the phenomena of development and of regeneration, has been made by Driesch.   It has been pointed out that in his *Analytische Theorie* Driesch assumed that development is due to "given" properties in the egg; that each stage is initiated by some substance contained in the egg acting on the stage that has just been completed.   That is, each stage is the condition of the following. The "rhythm" of development is accounted for in this way.   The changes are described as due to chemical processes (including also ferment actions).   The nucleus is supposed to contain all the different kinds of ferments that act, when set free, as stimuli on the protoplasm; but since the ferments are always set free at the propitious moment, Driesch was obliged to assume that the cytoplasm acts on the nucleus in such a way as to make it produce the proper ferment for the next stage.   Thus the cytoplasm first influences the nucleus, the latter sets free a specific ferment that starts a new chemical change in the cytoplasm, and the changed cytoplasm may then react again on the nucleus, and a different ferment be set free, etc.   Each change is therefore not only an effect of what has gone before, but the cause of the

next process.[1]  Driesch points out that it is necessary at this stage to make a further assumption, because the cytoplasm must not only be acted upon by the ferment, but it must itself be of such a sort that it *responds* to the action.  This leads to a great complication of the phenomena ; but the assumption does not depart, in the last analysis, from the idea of the cell as a system in a mechanical sense.  This assumption of a receiving and an answering station for the stimuli carries with it the further assumption of a many-sided "*harmony*." Without a harmony at each step in the development there could be no orderly ontogeny.  The assumption of this harmony introduces a new element into the series of hypotheses.  The *appearance* of a causal explanation was given in those parts of the argument preceding the introduction of the assumption of a harmony, but with the admission of this new element into the argument, the causal point of view is left. Driesch says in this connection : " If we cannot gain a singleness of view in the way that has been followed, we can reach this in another way.  Indeed, the way of doing so has been already implied in that part of the theory dealing with the harmony of the phenomena.  The existence of this harmony is inferred, because, in the large majority of cases, the ontogeny leads to a typical result.  Therefore we must assume that the conditions for the end result are given — the conditions are the harmony itself."  Put somewhat less obscurely, if more crudely, we may express Driesch's idea by saying that the harmony that stands for a hen is given in the hen's egg.

Driesch adds : " Because a typical result always follows, therefore every single step in the ontogeny must be judged, from an analytical standpoint, from the point of view of the result itself.  The result is the *purpose* of the ontogeny.  It is as though we visited daily a wharf where a ship is being built, — everything appears a chaos of single pieces, and we can only understand what we see when we consider what is to be made.  Only from a teleological point of view can we speak of a development, for this term expresses the very existence of an object to be developed.  The term is used fraudulently if it is intended to mean that the development is the outcome of 'processes,' using this term in the sense that a mountain or a delta develops from physical processes."  " We can only reach a satisfactory view of the phenomena when we introduce the word 'purpose.'  This means that we must look upon the ontogeny as a process carried out in its order and quality as though guided by an intelligence.  We arrive at this conclusion, because the individual whole is 'given,' as the clearly recognized goal of the entire process of development."

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[1] The importance of this conception is, in my opinion, marred by the fiction of the ferment action of the nucleus; but it should not be overlooked that Driesch avowedly called this a pure fiction.

In a later attempt to analyze the problem of development, Driesch examined it more fully from the point of view of the machine theory. This contribution must be looked upon rather as a *tour de force* that is intended to show how far this idea can be carried in its application to development.    Driesch explains that in his analytical theory he assumed from what is "given" in the egg that the egg can be understood causally, as a machine is understood, but what is "given" can be understood only teleologically.    He says: "What I defended was not vitalism, but, so far as the phenomena of life are concerned, exactly the current physico-chemical dogmatism; but I did not fail to see and to point out the consequences of this dogmatism, which every one (except Lotze) has avoided, viz., that the adaptive basis in which the living phenomena take place is 'given.'"    Driesch defines his view as formal-teleological, in contrast to vitalistic.    The former may also be called a machine theory of life in which the *purpose is given, not explained*.

In later writings Driesch has thrown over some of his earlier conclusions and adopted a causal-vitalistic philosophy.    The basis of this new conception is found in the proportional development of parts of an original whole, as has been explained in a preceding chapter. This result belongs to a category of phenomena that is in principle not machine-like, but of a specifically different kind.    It is something that cannot be explained by the agencies of the outer world, such as light, gravity, salinity, temperature, etc.    After examining other hypotheses, Driesch returns to a view that he had previously rejected, viz. the conception of "position," by which is meant the influence of the location in the whole.    This position has certain directions, but nothing in addition that is typical.    By the term "location in the whole" is meant that the word "location" (*Lage*) shall refer not to geometric space, but to the organization of the object that has its own directions.    A deformation of the whole may change very little the relative location of the parts.

In his earlier writings Driesch rejected this idea, because it did not seem to satisfy our etiological need, and also because he thought that he could reach his goal from the standpoint of initiating stimuli (*Auslösungen*).    Driesch now assumes that the stem of tubularia and the archenteron of the starfish, for example, have a polar structure. Bilateral forms, as the whole larva of the starfish, have a coördinated system of two axes with unlike poles and one axis with like poles, each of a given length or proportion.    The ends of the axes are characteristic points of the system.    If, in such a system, a typical act of differentiation appears, to which we can assign a cause, so far as the location is concerned, a change will occur as follows: To take the simplest case, that of a system with only one axis having unlike poles, as

the archenteron of the starfish, in which differentiation has not begun, we can picture to ourselves the formation of the divisions of the archenteron in a causal way by supposing the end of the axis, or pole, to be the location (*Sitz*) of an initiative "action at a distance" (*auslösende Fernkraft*). This locality, just because it is the end of a system, is something special; and it acts in such a way that wherever an effect is produced, it is the cause of that effect. This very way of looking at the problem postulates a sort of causal harmony. But how, it may be asked, can a special point or pole of an axis bring about an action in the system? This can be shown by means of a simple case, viz. the dividing up of the archenteron of the starfish into its characteristic parts. There are two effects produced, viz. the formation of the two constrictions of the wall. We need not consider the fact that the constrictions are formed, for this is established in the potence of the system, and is awakened by the initiating cause, but the place at which the constrictions are produced is that for which we should account. We must think of this cause as "action at a distance," and indeed as an "action at a distance" that works at a determinate, typical distance. This inherent measure of distance of the action is not one of absolutely fixed size, for a gastrula made shorter by an operation also subdivides into proportionate parts. The action starts from the poles of the system, and acts, not at an absolute, but at a relative distance, since it is dependent upon the length of the axis of the whole differentiating system. "The localization of ontogenetic processes is a problem *sui generis*. The phenomenon can always be expressed on the scheme of cause and effect, if we assume the 'action at a distance' to start from fixed points of a differentiating system."

In regard to the criterion of vitalistic phenomena Driesch makes the following statement: "On the current view we are inclined to see, in the formative changes, actual causes at work that even initiate those processes that we call stimuli; we do so because we pretend at present to know something of the special mechanism by which the formative changes work. The effects come into play through a causal union of simple processes of a physical-chemical sort that we may call a chain of stimuli. From the new point of view, the initiatory stimulus is not an initiatory cause or the effect of a causally united chemico-physical phenomenon. The stimulus is, from this point of view, a true stimulus, but the effect is not a true effect of its initiation, but is rather to be designated a responsive effect, for there is no connecting chain of stimuli. It is in the place of the latter that the vitalistic view appears. The only data of a machine sort in the conception are the arrangements for the reception and guidance of the stimulus, perhaps also the means for carrying out the response effect; for the machine data are only the prerequi-

sites of the phenomena, but in themselves do not bring about the result."

Driesch finds in this argument a *demonstration* of the vitalistic doctrine, but vitalism, of course, of a very special kind. Without a more elaborate presentation of his view it is not possible to give a detailed criticism of his conclusions; but a few of the more obvious objections that may be brought against this view may be discussed. The assumption of "action at a distance" does not, I think, in any way help to make the phenomenon clearer. The formation of a typical larva of normal proportions from a piece of an egg is just as mysterious after the assumption of an "action at a distance" of a proportionate sort as it was before. Driesch has introduced into the argument to establish a vitalistic standpoint one of the most obscure ideas of physical science. There is, so far as I can see, no necessity for such an assumption, since there is present in every case a continuous medium of protoplasm, which would seem to make this idea at least superfluous. Moreover, the additional element that Driesch has added to his conception of the process, namely, an action in proportion to the size of the piece, is objectionable if for no other reason than that it attributes to the unknown principle of "action at a distance" a quality that is the very thing that ought itself to be explained. This assumption, it seems to me, begs the entire question, and we can give no better explanation why it should belong to the principle of "action at a distance" than to anything else. Far from having given a demonstration of vitalism, Driesch has, I think, in his analysis simply set up an entirely imaginary principle, which, taken in connection with other undemonstrable qualities, is called vitalism.

If we cannot accept Driesch's demonstration of vitalism, from what point of view can we deal with the phenomenon of the production of a typical form from each kind of living material? Can we find a physico-chemical explanation of the phenomenon? Enough has been said to show that this property is one of the fundamental characteristics of living things and is, in all probability, a phenomenon which we certainly cannot at present hope to explain. Yet the question raised by Driesch is, at bottom, not so much whether we can give a physico-chemical explanation, but whether the phenomenon belongs to an entirely different class of phenomena from that considered by the physicist and by the chemist. Let us examine the results and see if we are really forced to conclude that there is no other physico-causal point of view possible.

In many cases in which a response to an external stimulus takes place, we must assume a physico-causal connection between the stimulus and the effect. The action of poisons, for instance, is an

example of this kind, and, in some cases, as in the formation of the galls of plants, the stimulus of a foreign body may lead to the development of a structure, the gall, of a definite form. The experiments of Herbst on the effect of lithium salts in sea water on the development of the sea-urchin embryo lead to a similar conclusion. The changes in form that result from other external agents, such as light, gravity, contact, etc., can be best understood from a physico-causal point of view, and it seems improbable at least that their action within the organ is transformed into a vitalistic causal action through Driesch's principle of an "action at a distance."[1] The effect of internal factors on the change of form is, however, much more difficult to deal with, since we know so little at present about these factors. Here we find amongst other phenomena that of the proportionate formation of a whole organ from a part of an old one, or of an egg. We find it difficult, if not impossible, to attribute this directly to external causes, yet, as I have tried to show, the first steps through which this takes place can be referred to physico-causal principles. These are the separation of the piece from the whole ; the change of the unsymmetrical piece into a symmetrical one, brought about, in part at least, by contractile phenomena in the piece, aided, no doubt, in some cases by surface tension, etc. These changes give the basis for the development of a new organization along the lines of structure that are already present in the piece. We find here the beginning of a physico-causal change, and, so far as I can see, we have no reason to suppose that at one stage in the process this passes over into the vitalistic-causal principle. It should, I think, be pointed out in this connection that even in the physical sciences it would not be difficult to establish a vitalistic principle, or whatever else it might be called, if we chose to take into account such properties of bodies as those which the chemist calls the affinities of atoms and molecules, or the symmetrical deposition of material on the surface of a crystal from a supersaturated solution, etc. These phenomena are usually looked upon as "given," that is, beyond the hope of possible examination. Until these questions are more fully understood scientists are, I think, justified in showing a certain amount of self-restraint in regard to the solution of such problems. Du Bois-Reymond has summed up this point of view in the dictum, "Ignorabimus," which is interpreted to mean, not only that we are ignorant at present on certain questions, but that we know we must remain ignorant. The formative changes in the organism appear to belong to this category of questions. This confession of ignorance need not mean that we cannot hope to discover the conditions under which the phenomena take place, so that we can predict with certainty what the results will be, but

[1] Not that Driesch supposes this would be the case.

the meaning of the change itself may remain forever obscure, at least from our present conception of physico-chemical principles. Shall we, therefore, call ourselves vitalists, because we find certain phenomena that we cannot hope to explain as the result of physical principles, or for which we must invent an unknown principle? Or can we succeed in demonstrating a different kind of principle in living things? If we could, we might be justified in calling ourselves by the name of vitalists. But who has made such a discovery? Does the well-known phenomenon of proportionate development give a demonstration of the unknown principle? Would one be justified in claiming a different principle that is not a physico-causal one, because the nerve impulse is different from any known physical phenomenon? The preceding pages have made clear, I hope, that, for my own part, I see no grounds for accepting a vitalistic principle that is not a physico-causal one, but perhaps a different one from any known at present to the physicist or chemist.

In order to make clear in what way certain terms have been used in the preceding chapters, it may not be out of place to indicate how it is intended that they should be employed. The word "cause" has been used in the sense in which the physicist uses the term. A "stimulus" is the chain of effects of a cause acting on a living body. In certain cases the cause itself may be spoken of as the stimulus, but only when its specific action on a living body is implied. A "factor" is a more general term and is usually one or more of a number of causes that produce a result. It may prove convenient to use this term where a change in form is produced. Thus the size of a piece is one of the factors that determines the result; the part of the body from which the piece is taken may also be a factor, or rather the kind of material contained in the piece. These examples will suffice to show that the word is used for an observed connection of a very general sort, especially for those cases in which we have not analyzed the factor into its components. The term is especially useful for cases in which the change in form is the outcome of the innate properties of the organization. The term may be used so that it need not prejudice the result, either in favor of a physico-causal or a vitalistic-causal point of view. It may be convenient to use it as an indifferent term in these respects. The word "force" I have attempted to avoid as far as possible, except in such current expressions as "the force of gravity," etc., for, apart from the loose way in which the word is used even by physicists, we know so little about the forces in the organism that it is best, I think, to use the word as sparingly as possible, and only where a known physical force can be shown to produce an effect.

Much misunderstanding has arisen in connection with the term "formative force." In the first place we naturally associate with this term the meanings attached to it by writers of the seventeenth and eighteenth centuries. They assumed a formative principle in living things, that is an expression of a formative force. Roux, who has more recently used the term, has attempted to avoid misunderstanding by using the plural, — "the formative forces of the organism"; but even under these circumstances, differences of opinion have arisen, as shown by the controversy between Roux ('97) and Hertwig ('94 and '97), on this point. A change in form carries with it a change of position of the parts, and the latter involves the idea of forces, but the nature of these forces is entirely obscure to us, at least we cannot refer them to any better-known category of physical or chemical forces. They may, perhaps, be most profitably compared to the forces of chemical union, but whether they are very numerous or can be reduced to a limited number of kinds of force, we do not know. If it could be shown that the changes in the organism are due to molecular changes, then the formative forces might appear to be only molecular forces, but we are not in position at present to demonstrate that this is the case, however probable it may appear.

Finally, the use of the term "organization" may be considered, although from what has been said already it is clear that there must be a certain amount of vagueness connected with our idea of what the organization can be. The organization, from the point of view that I have adopted, is a structure, or arrangement of the material basis of the organism, and to it are to be referred all the fundamental changes in form, and perhaps of function as well. We also use the term as applied to the completed structure, by which we mean that the organism consists of typical parts having a characteristic arrangement carrying out definite functions. When applied to the egg, or to a regenerating piece, the term refers to some more subtle structure that we are led to suppose to be present from the mode of behavior of the substance. As pointed out, we know this organization at present from only a few attributes that we ascribe to it, and are not in a position even to picture to ourselves the arrangement that we suppose to exist.

### REGENERATION AND ADAPTATION

One of the most difficult questions with which the biologist has to deal is the meaning of the adaptation of organisms to their environment. Pflüger, in an article entitled "The Teleological Mechanics of Living Nature," has drawn attention to the teleological character, or purposefulness, of certain processes in the living organism. "There

has been found only one general point of view, which if not absolute, yet is the rule, to account for the eternal transformations of energy in the living body. Only those combinations of causes take place that are as favorable as possible for the welfare of the animal. This holds true even when entirely new conditions are artificially introduced into the living organism. What is more remarkable than that, even in the highly organized mammal, there should be a regeneration of the bile duct after its removal, or that after a large piece of a nerve has been extirpated by a severe operation it should be again renewed? . . . What is more surprising than that the organism should become accustomed to the most diverse kinds of organic and inorganic poisons? . . . And, finally, there are a number of facts that make good the law that changes appear to be governed by no other principle than the purpose of making certain the existence of the organism."

Pflüger's teleological law of causality is that "the cause of every need of a living being is at the same time the cause of the fulfilment of the need." Pflüger explains that the word "cause" is here intentionally chosen in order to bring out the necessary, lawful connection in which the cause of each need stands in relation to the fulfilment of that need. He adds that it would have been more correct, but less pointed, to have said "motive" or "inducement" instead of "cause."

In order to illustrate what is meant by this law, the following examples may be given. Food and water bring back the organism to its normal condition. The absence of food in the body leads to hunger, and this to the taking in of more food; or, in other words, the need of food leads to the search for food, or at least to the taking in of food. The sexual desire, or the need to reproduce, brings about the condition of the animal that leads to reproduction. A defect in the valves of the heart leads to the enlargement of the right or the left ventricle. The removal of one kidney leads to the hypertrophy and increased function of the other. And although not explicitly stated by Pflüger in this place, we may add to this list the removal of a part of an animal, that leads to the regeneration of that part. Pflüger further states that we are making no subtle distinction when we point out that these phenomena, if looked at from the point of view of purposeful acts, appear to have a teleological side. In reply to this it may be stated, however, that in certain cases of regeneration it can be shown that the result is entirely useless, or even injurious to the organism; hence the teleological nature of the process is entirely lost sight of, and we are the more ready to accept a simple causal explanation of the phenomena. The best example of this that I can give is the development of a tail at the anterior end of a posterior piece of an earthworm. This process is not an occasional one, but is constant. An example of an apparently useful result, so

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far as the individual's well-being is concerned, but entirely useless from the point of view of the continuance of the species, is found in the development, in the earthworm, of a new head after the removal of the anterior end, including the reproductive region.   New reproductive organs are not formed, and, although, in virtue of the regeneration of a new head, the individual is capable of carrying on its existence, yet the race of earthworms is not thereby benefited.   The production of two tails in lizards, or of two or more lenses in the eyes of newts, are examples of the regeneration of superfluous structures.

If, however, it is claimed that in the large majority of cases the process of regeneration is for the welfare of the individual, and for the race also, this must be admitted, and it is this fact which has made a deep impression on the minds of many biologists.

From the causal point of view, we may look upon the formative changes as the necessary outcome of strictly causal principles, and we may suppose that they take place without respect to the final result.   But the question before us is rather to explain, if possible, why the changes that take place are in so many cases useful ones. That they are not always useful must be admitted, that they sometimes are must be granted, and it is the latter alternative that has attracted special attention.   Now it is undoubtedly the simplest solution to claim that the scientist has nothing to do with the adaptiveness of the response, that his whole problem lies in a study of the causal phenomena involved in each process, but it is unquestionably true that scientists have not been satisfied to confine their hypotheses to this side of the question.   The widespread interest in the theory of natural selection is, I think, due to the fact that it appears to offer an explanation of the formation of adaptive processes — not that it pretends to explain the origin of the adaptive structures or processes themselves, but that it seems to account for the adaptiveness of the fully formed product, *i.e.* the organism.   For it will be seen that if only those forms (variations) survive that are useful, and survive either because the environment selects them (and exterminates the others), or because new forms that arise find a new place in nature where they can remain in existence, then the adaptiveness of the form to its surroundings would seem to be accounted for.   In this case we can see how the causal processes that take place in the organism need have no causal connection with the environment, — except in the sense that the environment has acted as a selective agent, and appears, therefore, in the light of a teleological factor.   But, as has been said before, the question is not so much that organisms *are* adapted, as that organisms *respond adaptively* to changes to which they can never have been subjected before.   It is for the latter fact that a solution is to be sought.

In this whole question there is danger of extending our own experience as agents in the constructing of products useful to ourselves, to the organic world, in attempting to account for the way in which the useful characters of organisms have arisen. We see a ship being built, and we know that when it is finished it will be useful. We explain its building by its future usefulness, — that is, we explain the process as the result of human teleology. But have we any right to extend this principle to the organic world, and infer that processes are there carried out *because* they will ultimately be useful to the individual in which they take place? Unconsciously we have shifted our point of view. The ship does not build itself, and the final result of the building is of no use to the ship. On the contrary, the organism does build itself and the result is useful only to itself. Unless we suppose that some external agent acting as we do ourselves directs the formative processes in animals and plants, we are not justified in extending our experience as directive agents to the construction of the organic world; and if we are not justified in drawing such a conclusion, since the organism by no means always responds adaptively, and in many cases very badly and incompletely, then, it seems to me, we must look for another point of view.

In connection with his work on the regeneration of the eye of the salamander, Gustav Wolff ('93) has made some sweeping statements in regard to the phenomenon of adaptation. "Purposeful adaptation is that which makes the organism an organism. It is this adaptation that appears to us as the most characteristic property of all living things. We can think of no organism without this characteristic." In another place he states, " . . . we recognize that every explanation that presupposes the living being, every post-vital explanation of organic adaptation, presupposes in every case that which it attempts to explain; we recognize that the explanation of adaptation must coincide with the explanation of life itself." There is, perhaps, some truth in this statement, but, on the other hand, Wolff has, I think, shot somewhat over the mark. As Fischel (1900) has pointed out, the response is sometimes not adaptive, as when two lenses develop in the same eye in the salamander; and, we may add, as when an antenna develops in certain crustacea in place of an eye, or as when a tail develops instead of a head, or a head in place of a tail. In the light of these facts, it is, I think, going too far to assert that the power of living things to respond adaptively to changes in themselves or in their environment is synonymous with life itself. All that we can fairly claim is that in several cases living forms have been shown to be able to *complete themselves*, and this may be *interpreted* as an adaptive response. It would carry us far beyond the scope of the present volume to discuss the question of adaptation in general, and I think it

highly probable that it will prove true that there are many kinds of adaptive responses that must be considered separately and each on its own merits. Let us, therefore, confine our concluding remarks entirely to *regenerative changes* which, after they have been completed, are for the good of the organisms. Our preceding discussion has led to the conclusion that the phenomena of regeneration are not processes that have been built up by the accumulation of small advances in a useful direction; that they cannot be accounted for by the survival of those forms in which the changes take place better than in their fellows, for it is often not a question of life and death whether or not the process takes place, or even a question of leaving more descendants. On the contrary, it seems highly probable that the regenerative process is one of the fundamental attributes of living things, and that we can find no explanation of it as the outcome of the selective agency of the environment. The phenomena of regeneration appear to belong to the general category of growth-phenomena, and as such are characteristic of organisms. Neither regeneration nor growth can be explained, so far as I can see, as the result of the usefulness of these attributes to the bodies with which they are indissolubly associated. The fact that the process of regeneration is useful to the organism cannot be made to account for its existence in the organism.

# LITERATURE

**Aldrovandus, Ulysses.**
1642. Historia Monstrorum. MDCXLII. Cap. VIII.
1645. Patritii boloniensis de quadrupedibus digitatis oviparis. Lib. II. Boloniae, MDCXXXXV.

**Allman, J. A.**
'64. Report of the present State of our Knowledge of the Reproductive System in the Hydroida. Report of the 33d Meeting of the British Assoc., 1864.

**Andrews, E. A.**
'90. Autotomy in the Crab. The American Naturalist, XXIV, 1890.
'91. Report upon the Annelida Polychaeta of Beaufort, North Carolina. Proc. U. S. National Museum, XV, p. 286, 1891.

**Andrews, G. F.**
'97. Some Spinning Activities of Protoplasm, etc. Jour. Morph., XII, 1897.

**Apostolides, N. Christo.**
'82. Anatomie et développement des Ophiures. Arch. Zool. Expérim., X, 1882.

**Aristotle.**
Historia de animalibus, Julio Caesare, Scaligero interprete, cum ejusdem Commentariis. Tolosae, MDCXIX, Lib. II, Cap. XX.

**Arnoult de Nobleville et Salerne.**
1756. Suite de la matière médicale de Geoffroy, t. 12, MDCCLVI.

**Aschoff, L.**
'95. Regeneration und Hypertrophie. Ergebnisse d. allg. Path. Morph. und Physiol., 1895.

**Balbiani, E. G.**
'88. Recherches expérimentales sur la mérotomie des infusoires ciliés. Recueil zool. de la Suisse, V, 1888.
'91. Sur les régénérations successives du peristome, etc., chez les stentors, etc. Zool. Anz., 1891.
'91. Nouvelles recherches expérimentales sur la mérotomie des infusoires ciliés. Arch. microgr., IV et V, 1891–93.

**Bardeen, C. R.**
'01. On the Physiology of the Planaria maculata, etc. Am. Jour. Physiol., V, 1901.

**Barfurth, D.**
'91–'00. Regeneration. Ergebnisse Anat. und Entwickl. Merkel und Bonnet, 1891–1900.
'91. Versuche zur funktionellen Anpassung. — Zur Regeneration der Gewebe. Arch. f. Mikr. Anat., XXXVII, 1891.
'93. Experimentelle Untersuchungen über die Regeneration der Keimblätter bei den Amphibien. Anat. Hefte, IX, 1893.
'94. Die Experimentelle Regeneration überschüssiger Gliedmassenteile bei den Amphibien. Arch. f. Entw.-mech., I, 1894.
'99. Sind die Extremitäten der Frösche regenerationsfähig? Arch. f. Entw.-mech., IX, 1899.
'99. Die Experimentelle Herstellung der Cauda bifida bei Amphibienlarven. Arch. f. Entw.-mech., IX, 1899.

**Barrois, J.**
  '77.  Mémoire sur l'embryologie des némertes.  Ann. Sc. Nat. (6), tome VI, 1877.
**Bateson, W.**
  '94.  Materials for the Study of Variation, 1894.
**Baudelot, E.**
  '69.  De la régénération de l'extrémité céphalique chez le Lombric terrestre.  Bull. Soc. d. Sc. Nat., Strassbourg, II, 1869.
**Benham, W. B.**
  '96.  Fission in Nermertines.  Q. J. Micr. Sc., XXXIX, 1896.
**Bergh, R. S.**
  '96.  Über den Begriff der Heteromorphose.  Arch. f. Entw.-mech., III, 1896.
**Bert, P.**
  '60.  Recherches Expérimentales.  Ann. d. Sc. Natur. (5 Ser.), V, 1860.
**Bickford, E. E.**
  '94.  Notes on Regeneration and Heteromorphosis in Tubularian Hydroids.  Journ. Morph., IX, 1894.
**Blumenbach.**
  1787.  Specimen physiologiae comparatae inter animantia calidi et frigidi sanguinis; in commentationes soc. reg. scient. Gottingensis, Vol. VIII.  Gottingae, 1787.
**Bock, M. von.**
  '97.  Über die Knospung von Chaetogaster diaphanus.  Jena. Zeit. f. Naturw., XXXI, 1897.
**Bonnet, C.**
  1745.  Traité d'insectologie.  Seconde partie.  Observations sur quelques espèces de vers d'eau douce, qui coupés par morceux, deviennent autant d'animaux complets. Paris, 1745.
**Bordage, E.**
  '97.  Phénomènes d'autotomie observés chez les Nymphes de Monandroptera inuncans et de Raphiderus scabrosus.  Compt. Rend. des séances de la Soc. de Biologie.  Paris, 1897.
  '97.  Sur la régénération tétramérique du tarse des Phasmides.  *Ibid.*, 1897.
  '98.  Sur les localisation des surfaces de régénération chez les Phasmids.  *Ibid.*, 1898.
  '98.  Cas de régénération du bec des oiseaux expliqué par la loi de Lessona.  *Ibid.*, 1898.
  '99.  Régénération des membres chez les Mantides, etc.  *Ibid.*, XXVIII, 1899.
  '99.  Sur le mode probable de formation de la soudure-fémoro-trochantérique chez les Arthropodes.  *Ibid.*, XXVIII, 1899.
  '00.  On the Absence of Regeneration in the Posterior Limbs of the Orthoptera Saltatoria and its Probable Causes.  Ann. and Mag. of Nat. Hist., 1900.
  '00.  Regeneration of the Tarsus and of the Two Anterior Parts of Limbs in the Orthoptera Saltatoria.  *Ibid.*, 1900.
**Born, G.**
  '97.  Über Verwachsungsversuche mit Amphibienlarven.  Arch. f. Entw.-mech., IV, 1897.
**Boulenger, G. A.**
  '88.  On the Scaling of the Reproduced Tail in Lizards.  Proc. Zool. Soc., London, 1898.
**Boveri, Th.**
  '89.  Ein geschlechtlich erzeugter Organismus ohne mütterliche Eigenschaften.  Sitzungsber. Ges. Morph. Phys. München , V, 1889.
  '95.  Über die Befruchtungs- und Entwickelungsfähigkeit kernloser Seeigeleier.  Arch. f. Entw.-mech., II, 1895.
  '01.  Über die Polarität des Seeigel-Eies.  Verhand. d. Phys.-Med. Gesell. Würzburg (N. F.), XXXIV, 1901.
**Brand, F.**
  '96.  Fortpflanzung und Regeneration von Lemanea fluviatilis.  Berichte d. deutsch. botan. Gesell., V, 1896.

**Brefeld, O.**
    '77.  Die Entwickelungsgeschichte der Basidiomyceten.  Botan. Zeit., 1876.
    '77.  Botanische Untersuchungen.  Schimmelpilze, III (page 69), 1877.

**Brindley, H. H.**
    '97.  On the Regeneration of Legs in the Blattidae.  Proc. Zool. Soc., London, 1897.
    '98.  On certain Characters of Reproduced Appendages in Arthropoda, particularly in the Blattidae.  *Ibid.*, 1898.

**Broussonet, M.**
    1786.  Observations sur la régénération de quelques parties du corps des Poissons.  Hist. d. l'Acad. Roy. des Sciences, 1786.

**Bülow, C.**
    '82.  Über Theilungs- und Regenerations-vorgänge bei Würmern.  Arch. Naturg., XLIX, 1882.
    '83.  Die Keimschichten des wachsenden Schwanzendes von Lumbriculus variegatus, etc. Zeit. Wiss. Zool., XXXIX, 1883.
    '83.  Über anscheinend freiwillige und künstliche Theilung mit wechselnder Regeneration bei Coelenteraten, Echinodermen, und Vermes.  Biol. Centralbl., III, 1883–84.

**Byrnes, Esther F.**
    '98.  On the Regeneration of Limbs in Frogs after the Extirpation of Limb Rudiments. Anat. Anz., XV, 1898.

**Cadiat, O.**
    '76.  Du cristallin, anatomie et développement, usage et régénération.  Thèse d'agrégation.  Paris, 1876.

**Cardanus, Hieronymus.**
    1580.  Mediolanensis, medici, de subtilitate.  Lugundi, MDLXXX.

**Carnot, P.**
    '99.  Les régénérations d'organs.  Paris, 1899.

**Carriere, J.**
    '80.  Studien über die Regenerations-Erscheinungen bei den Wirbellosen.  Würzburg, 1880.

**Chabry, L.**
    '87.  Contribution à l'embryologie normale et tératologique des ascidies simples.  Journ. Anat. et Phys., XXIII, 1887.

**Chantran, S.**
    '73.  Expériences sur la régénération des yeux chez les écrevisses.  Compt. rend., LXXVI, 1873.

**Chun, C.**
    '92.  Die Dissogonie der Rippenquallen.  Festschr. f. Leuckart, 1892.

**Colucci, V. S.**
    '85.  Studio sperimentale sulla rigenerazione degli arti e della coda nei Tritoni.  Rendeconto delle sessioni della R. Accad. d. Scienze dell' Ist. di Bologna, 1885.
    '91.  Sulla regenerazione parziale dell' occhio nei Tritoni.  Memorie della R. Accad. delle Scienze dell' Ist. di Bologna (Ser. V), I, 1891.

**Conklin, E. G.**
    '98.  Environmental and Sexual Dimorphism in Crepidula.  Proc. Acad. Nat. Science, Philadelphia, 1898.

**Contijan.**
    '90.  Sur l'autotomie chez la Sauterelle et le Lezard.  Compt. rend., 1890.

**Coutière, H.**
    '98.  Notes sur quelques cas de régénération hypotypique chez Alpheus.  Bull. Soc. Ent., France, 1898.

**Crampton, H. E.**
    '96.  Experimental Studies on Gasteropod Development.  Arch. f. Entw.-mech., III, 1896.
    '97.  The Ascidian Half-Embryo.  New York Acad. of Sc., X, 1897.

**Dalyell, J. G.**
'14.  Observations on Some Interesting Phenomena in Animal Physiology, exhibited by Several Species of Planariae.  Edinburgh, 1814.
'47.  Rare and Remarkable Animals in Scotland.  London, 1847–48.
'51.  Powers of the Creator, 1851.

**Darwin, C.**
'54.  Monograph of the Cirrepedia, 1854.
'68.  The Variation of Animals and Plants under Domestication, 1868.

**Davenport, C. B.**
'93.  Studies in Morphogenesis.  I. On the Development of the Cerata in Aeolis.  Bull. Mus. Comp. Zool., XXIV, 1893.
'94.  Studies in Morphogenesis.  Nr. 2.  Regeneration in Obelia and its Bearing on Differentiation in the Germ-plasma.  Anat. Anz. 9, 1894.
'97.  Experimental Morphology, I and II.  New York, 1897–99.

**Dawydoff, C.**
'01.  Beiträge zur Kenntnis der Regenerations Erscheinungen bei den Ophiuren.  Zeit. Wiss. Zool., LXIX, 1901.

**Delage, Y.**
'95.  La Structure de Protoplasma et les Théories sur L'Hérédité, 1895.
'99.  Études sur la Merogonie.  Arch. de Zool. expérim. et générale, 1899.

**Dendy, A.**
'56.  On the Regeneration of the Visceral Mass in Antedon Rosaceus.  Stud. Biol. Lab., Owens College, I, 1856.

**Dewitz, H.**
'94.  Über das Abwerfen der Scheeren des Flusskrebses.  Biol. Centralb., V, 1894.

**Driesch, H.**
'90.  Heliotropismus bei Hydroidpolypen.  Zool. Jahrb. (Syst. Abt.), V, 1890.
'91.  Die Stockbildung bei den Hydroidpolypen und ihre theoretische Bedeutung.  Biol. Cent., XI, 1891.
'91.  Die mathematisch-mechanische Betrachtung morphologischer Probleme der Biologie.  Jena, 1891.
'91–'93.  Entwickelungsmechanische Studien.
'91.  I. Der Wert der beiden ersten Furchungszellen in der Echinodermenentwickelung.  Zeit. f. wiss. Zool., LIII, 1891.
'91.  II. Über die Beziehungen des Lichtes zur ersten Etappe der tierischen Formbildung.  *Ibid.*
'92.  III. Die Verminderung des Furchungsmaterials und ihre Folgen.  Zeit. f. wiss. Zool., LV, 1892.
'92.  IV. Experimentelle Veränderungen des Typus der Furchung und ihre Folgen.  *Ibid.*
'92.  V. Von der Furchung doppelbefurchteter Eier.  *Ibid.*
'92.  VI. Über einige allgemeine Fragen der theoretischen Morphologie.  *Ibid.*
'93.  VII. Exogastrula und Anenteria.  Mitt. zool. Stat.  Neapel, II, 1893.
'93.  VIII. Über Variation der Micromerenbildung.  *Ibid.*
'93.  IX. Über die Vertretbarkeit der " Anlagen " von Ektoderm und Entoderm.  *Ibid.*
'93.  X. Über einige allgemeine entwicklungsmechanische Ergebnisse.  *Ibid.*
'92.  Kritische Erörterungen neuerer Beiträge zur theoretischen Morphologie.  II. Zur Heteromorphose der Hydroidpolypen.  Biol. Cent., XII, 1892.
'93.  Zur Verlagerung der Blastomeren des Echinideneies.  Anat. Anz., VIII, 1893.
'93.  Zur Theorie der tierischen Formbildung.  Biol. Cent., XIII, 1893.
'93.  Die Biologie als selbständige Grundwissenschaft.  Leipzig, 1893.
'94.  Analytische Theorie der organischen Entwickelung.  Leipzig, 1894.  (Also Arch. f. Entw.-mech., IV, 1896.)
'95.  Von der Entwickelung einzelner Ascidienblastomeren.  Arch. f. Entw.-mech., I, 1895.

'95. Zur Analysis der Potenzen embryonaler Organzellen. Arch. f. Entw.-mech., II, 1895.

'96. Die Maschinentheorie des Lebens. Biol. Cent., XVI, 1896.

'96. Über den Anteil zufälliger individueller Verschiedenheiten an ontogenetischen Versuchsresultaten. Arch. f. Entw.-mech., III, 1896.

'96. Die taktische Reizbarkeit der Mesenchymzellen von Echinus microtuberculatus. Arch. f. Entw.-mech., III, 1896.

'96. Betrachtungen über die Organisation des Eies und ihre Genese. Arch. f. Entw.-mech., IV, 1896.

'96. Über einige primäre und sekundäre Regulationen in der Entwickelung der Echinodermen. Arch. f. Entw.-mech., IV, 1896.

'96. Zur Analyse der Reparationsbedingungen bei Tubularia. Vierteljahrsschr. Nat. Ges., Zürich, XVI, 1896.

'97. Über den Wert des biologischen Experiments. Arch. f. Entw.-mech., V, 1897.

'97. Neuere Beiträge zur exakten Morphologie in englischer Sprache. III (1896). Arch. f. Entw.-mech., V, 1897.

'97. Studien über das Regulationsvermögen der Organismen. I. Von den Regulationen Wachstums- und Differenzierungsfähigkeiten der Tubularia. Arch. f. Entw.-mech., V, 1897.

'97. Von der Beendigung morphogener Elementarprozesse. Arch. f. Entw.-mech., V, 1897.

'98. Über rein mütterliche Charactere an Bastardlarven von Echiniden. Arch. f. Entw.-mech., VII, 1898.

'99. Von der Methode der Morphologie. Biol. Cent., XIX, 1899.

'99. Die Lokalisation morphogenetischer Vorgänge. Ein Beweis vitalistischen Geschehens. Arch. f. Entw.-mech., VIII, 1899.

'99. Studien über das Regulationsvermögen. II. Quantitative Regulationen bei der Reparation der Tubularia. Arch. f. Entw.-mech., IX, 1899. III. Notizen über die Auflösung und Wiederbildung des Skeletts von Echinidenlarven. *Ibid.*

'00. Die isolirten Blastomeren des Echinidenkeimes. Arch. f. Entw.-mech., X, 1900.

'00. Studien über das Regulationsvermögen der Organismen. IV. Die Verschmelzung der Individualität bei Echinidenkeimen. Arch. f. Entw.-mech., X, 1900.

'99. Resultate und Probleme der Entwickelungsphysiologie der Thiere. Ergebn. d. Anat. u. Entw. (1898), 1899.

'01. Studien über das Regulationsvermögen der Organismen. V. Ergänzende Beobachtungen an Tubularia. Arch. f. Entw.-mech., XI, 1901.

**Driesch, H. and Morgan, T. H.**

'95. Zur Analysis der ersten Entwickelungsstadien des Ctenophoreneies. Arch. f. Entw.-mech., II, 1895. (Also Driesch : Bemerkungen, etc., Zool. Anz., 1896.)

**Dugès, A.**

'28. Recherches sur la circulation, la respiration et la reproduction des Annélides abranches. Annales des Sci. nat. (5), XVI, 1828.

'29. Mémoire sur les espèces indigènes du genre Lacerta. Annales des Sciences naturelles, XVI, 1829.

**Duméril, A.**

'67. Expériences démontrant que la vie aquatique des Axolotle abranchies extérieurs se continue après l'ablation des louppes branchiales. Nouvelles Archives du Museum. III, 1867.

**Duyne, J. van.**

'96. Über Heteromorphose bei Planarien. Pflüger's Arch., LXIV, 1896.

**Ehlers, E.**

'69. Die Neubildung des Kopfes und der vorderen Körpertheile bei polychaeten Anneliden. Erlangen, 1869.

'99. Palolo. Biol. Centralb., XIX, 1899.

**Eimer, Th.**

'73. Über Künstliche Theilbarkeit von *Aurelia aurita* und *Cyanea capillata.* Verh. d. phys.-med. Gesell. zu Würzburg (N. F.), VI (Dec.), 1873.

**Emery, C.**

'97. Wer hat die Regeneration der Augenlinse aus dem Irisepithel zuerst erkannt und dagestellt ? Anat. Anz., XIII, 1897.

**Endres, H.**

'95. Anstichversuche an Eiern von Rana fusca. II. Theil. Arch. f. Entw.-mech., II, 1895-96.

'95. Über Anstich- und Schnürversuche an Eier von Triton taeniatus. 73 Jahreb. d. Schles. Ges. f. Vaterl. Kultur, 18 Juli, 1895.

**Endres, H., and Walter, H. E.**

'95. Anstichversuche an Eiern von Rana fusca. I. Theil. Arch. f. Entw.-mech., II, 1895.

**Fiedler, K.**

'91. Entwickelungsmechanische Studien an Echinodermeiern. Festschr. Nägeli u. Kölliker, Zurich, 1891.

**Fischel, A.**

'97. Experimentelle Untersuchungen am Ctenophorenei, 1-4. Arch. f. Entw.-mech., VI, 1897-98.

'98. Über die Regeneration der Linse. Anat. Anz., XIV, 1898.

**Flemming, W.**

'80. Über Epithelregeneration und sogen. freie Kernbildung. Arch. f. mikr. Anat., XVIII, 1880.

**Flexner, S.**

'98. The Regeneration of the Nervous System of Planaria torva and the Anatomy of the Nervous System of Double-headed Forms. Jour. Morph., XIV, 1898.

**Forest-Heald, F. de.**

'98. A Study of Regeneration as exhibited by Mosses. Bot. Gaz., XXVI, 1898.

**Fraisse, P.**

'85. Die Regeneration von Geweben und Organen bei den Wirbelthieren, besonders bei Amphibien und Reptilien. Kassel und Berlin, 1885.

**Fredericq, L.**

'83. Sur l'autotomie ou mutilation par voie réflexe comme moyen de défense chez les animaux. Arch. d. Zool. expérim. (Ser. 1), 1883.

'87. L'autotomie chez les étoiles de mer. Revue Scientifique (Ser. 3), XIII, 1887.

'93. L'autotomie ou la mutilation dans le règne animal. Bull. de l'Acad. roy. de Belgique (Ser. 3), XXVI, 1893.

**Frenzel, J.**

'91. Über die Selbstverstümmelung (Autotomie) der Thiere. Arch. f. d. Ges. Physiol., L, 1891.

**Friedländer, B.**

'95. Über die Regeneration herausgeschnittener Theile des Central nerven-systems von Regenwürmern. Zeit. f. Wiss. Zool. LX, 1895.

'98. Uber den sogennanten Palolo-wurm. Biol. Cent., XVIII, 1898.

'99. Nochmals der Palolo, etc. Biol. Centralbl., XIX, 1899.

**Fuhrmann, M.**

'98. Sur les phénomènes de la régénération chez les Invertébrés. Arch. Sc. Nat., V, 1898.

**Gachet, M. H.**

'34. Mémoire sur la reproduction de la queue des reptiles sauriens. Actes de la société linnéenne de Bordeaux, Nr. 36, 25 Juillet, 1834.

**Gayat, M. J.**

'73. Experimentalstudien über Linsenregeneration. Klin. Monatsbl. für Augenheilk., 1873.

Gesner, Conrad.
  1686.  Historiae animalium.  Lib. II, MDCLXXXVI.
Giard, A.
  '95.  Polydactylie provoquée chez Pleurodèles Walthii Mich.  Compt. Rend. Soc. Biol., II, 1895.
  '96.  Y a-t-il antagonisme entre la " Greffe " et la " Régénération."  *Ibid.*, 1896.
  '97.  Sur les régénérations hypotypiques.  *Ibid.*, IV, 1897.
  '97.  Sur l'autotomie parasitaire, etc.  *Ibid.*, 1897.
Glückselig, M. Ch.
  '63.  Über das Leben der Eidechsen, Verhandl. d. zool.-bot. Vereins in Wien., XIII, 1863.
Godelmann, R.
  '01.  Beiträge zur Kenntniss von Bacillus Rosii Fabr. mit besonderer Berüchsichtigung der bei ihm vorkommenden Autotomie und Regeneration einzelner Gliedmassen. Arch. f. Entw.-mech., XII, 1901.
Goebel, K.
  '98.  Organographie der Pflanzen.  I. Allgemeine Organographie, Jena, 1898.
Goette, A.
  '69.  Über Entwickelung und Regeneration des Gliedmassenskeletts der Molche.  Tübingen, 1869.
Gonin, J.
  '96.  Étude sur la Régénération du cristallin.  Ziegler's Beiträge z. pathol. Anat., XIX, 1896.
Goodsir, H. D. S.
  '44.  A Short Account of the Mode of Reproduction of Lost Parts in the Crustacea. Ann. and Mag. Nat. Hist., XIII, 1844.
Graber, V.
  '67.  Zur Entwickelungsgeschichte und Reproductionsfähigkeit der Orthopteren.  Berichte d. kaiserl. Akad. d. wiss. Wien.  LV, 1867.
Greef, R.
  '67.  Über Actinosphaerium Eichhornii, etc.  Arch. f. Mikr. Anat., III, 1867.
Griffini e Marchio.
  '99.  Sulla rigenerazione totale della retina nci tritoni.  Riforma med., 1899.
  '99.  Sur la régénération de la rétine chez les tritons.  Arch. ital. de Biolog., XII.
Gruber, A.
  '84-'5.  Über Künstliche Theilung bei Infusorien, I.  Biolog. Centralbl., IV, 1884–85.
  '85-'6.  Same, Part II.  *Ibid.*, V, 1885–86.
  '86.  Beiträge zur Kenntniss der Physiologie und Biologie der Protozoen.  Ber. Nat. Ges. Freiburg, I, 1886.
  '87.  Mikroskopische Vivisektion.  Ber. d. Naturfor. Gesell. zu Freiburg, II, 1887.
Haeckel, E.
  '68.  Monographie der Moneren.  Jena Zeit. f. Naturwiss., IV, 1868.
  '69.  Entwickelungsgeschichte der Siphonophoren (page 73), 1869.
  '78.  Die Kometenform der Seesterne und der Generationswechsel der Echinodermen. Zeit. f. wiss. Zool., XXX, 1878.
Hargitt, C. W.
  '97.  Recent Experiments on Regeneration.  Zool. Bull., I, 1897.
  '99.  Experimental Studies upon Hydromedusae.  Biolog. Bull., I, 1899.
Harrison, R. G.
  '98.  The Growth and Regeneration of the Tail of the Frog Larva.  Arch. f. Entw.-mech., VII, 1898.
Hasse, H.
  '98.  Über Regeneration bei Tubifex rivulorum.  Zeit. wiss. Zool., LXV, 1898.
Hazen, A. P.
  '99.  The Regeneration of a Head instead of a Tail in an Earthworm.  Anat. Anz., XVI, 1899.

**Heider, K.**
    '97. Ist die Keimblätterlehre erschüttert? Zool. Centralb., IV, 1897.

**Heineken, C.**
    '28–'29. Experiments and Observations on the Casting off and Reproduction of the Legs in Crabs and Spiders. The Zool. Journal, IV, 1828–29.

**Hepke, P.**
    '97. Über histo- und organogenetische Vorgänge bei den Regenerationsprozessen der Naiden. Zeit. wiss. Zool., LXV, 1897.

**Herbst, C.**
    '94. Über die Bedeutung der Reizphysiologie für die kausale Auffassung von Vorgängen in der tierischen Morphologie. Biol. Centralb., XIV und XV, 1894 u. 1895.
    '95–'99. Über die Regeneration antennenähnlicher Organe an Stelle von Augen I. Arch. f. Entw.-mech., II, 1895.
    '96. II. Versuche an Sicyonia sculpta. Vierteljahrsschr. d. Naturf.-Ges., Zurich, 1896.
    '99. III u. IV. Weitere Versuche, u. s. w. Arch. f. Entw.-mech., IX, 1899.
    '96. Experimentelle Untersuchungen über den Einfluss der veränderten chemischen Zusammensetzung, etc. Arch. Entw.-mech., II, 1896.
    '97. Über die zur Entwickelung der Seeigellarven nothwendigen anorganischen Stoff, I. *Ibid.*, V, 1897.

**Herculais, K. d'.**
    '75. Recherches zur l'organisation et la developpement des volucelles, 1875.

**Herlitzka, A.**
    '96. Contributo allo studio della capacita evolutiva dei due primi blastomeri nell' uovo di tritoni (triton cristatus). Arch. f. Entw.-mech., II, 1896.

**Herrick, F. H.**
    '95. The American Lobster. Bull. U. S. Fish Commission, 1895.

**Hertwig, O.**
    '85. Das Problem der Befruchtung und der Isotropie des Eies. Jena Zeit., XVIII, 1885.
    '85. Welchen Einfluss übt die Schwerkraft auf die Teilungen der Zellen? *Ibid.*, 1885.
    '90. Experimentelle Studien am tierischen Ei vor, während und nach der Befruchtung. *Ibid.*, XXIV, 1890.
    '92. Urmund und Spina bifida. Arch. f. mikr. Anat. XXXIX, 1892.
    '92. Ältere und neuere Entwickelungstheorien. Rede. Berlin, 1892.
    '93. Über der Wert der ersten Furchungszellen für die Organbildung des Embryo. Arch. f. mikr. Anat. XLII, 1893.
    '94. Zeit- und Streitfragen der Biologie, I. Präformation oder Epigenesis? Jena, 1894.
    '95. Beiträge zur experimentellen Morphologie und Entwickelungsgeschichte. I. Die Entwickelung des Froscheies unter dem Einfluss schwächerer und stärkerer Kochsalzlösungen. Arch. f. mikr. Anat., XLIV, 1895.
    '96. Experimentelle Erzeugung tierischer Missbildung. Festschr. Gegenbaur., II, 1896.
    '97. Zeit- und Streitfragen, II. Mechanik und Biologie, Jena, 1897.
    '98. Über den Einfluss der Temperatur auf die Entwickelung von Rana fusca und Rana esculenta. Arch. f. mikr. Anat., LI, 1898.
    '98. Die Zelle und die Gewebe. II. Allgemeine Anatomie und Physiologie der Gewebe. Jena, 1898.
    '98. Beiträge, etc., IV. Über einige durch Centrifugalkraft in der Entwickelung des Froscheies hervorgerufene Veränderungen. Arch. f. mikr. Anat., LIII, 1898.

**Hescheler, K.**
    '96–'98. Über Regenerationvorgänge bei Lumbriciden, I u. II. Jena. Zeit., XXX, 1896, und XXXI, 1898.

**Hirota, S.**
    '95. Anatomical Notes on the "Comet" of Linkia Multifora. Zool. Mag. Tokyo, VII, 1895.

**His, W.**
    '75. Unsere Körperform und das physiologische Problem ihrer Entstehung. Leipsig, 1875.

**Hofer, B.**
'89. Experimentelle Untersuchungen über den Einfluss des Kerns auf das Protoplasma. Jena. Zeitsch. f. Naturf. (N. F.), XVII, 1889.

**Horst, R.**
'86. Zur Regenerationslitteratur. Zool. Anz., IX, 1886.

**Hoy, P. R.**
'71. The Development of Amblystoma lurida. The American Naturalist, 1871.

**Hubrecht, A. A. W.**
'87. Report on the Nemertines. Reports of the Challenger Expedition, 1887.

**Ischikawa, C.**
'90. Trembley's Umkehrungsversuche an Hydra nach neuen Versuchen erklärt. Zeit. f. wiss. Zool., XLIX, 1890.

**Joest, E.**
'95. Transplantationsversuche an Regenwürmern. Sitz. ber. d. Gesell. z. Berf. d. ges. Naturwiss. zu Marburg, 1895.
'97. Transplantationsversuche an Lumbriciden. Arch. f. Entw.-mech. V, 1897.

**Johnstonus, Joannes.**
1657. Historiae naturalis de quadrupedibus. Amstelodami, MDCLVII, t. I, lib. IV, c. II, art. I u. art. II.

**Kennel, J. von.**
'82. Über Teilung und Knospung der Tiere. Dorpat, 1882.
'82. Über Ctenodrilus pardalis. Arb. a. d. zool. zoot. Inst. Würzburg, V, 1882.
'88. Biologische und Faunistische Notizen aus Trinidad. Arb. d. Zool.-Zoot. Inst., Würzburg, VI, 1888.

**Kinberg, J. G. H.**
'67. Om regeneration af hufvudet och de främre segmenterna hosen Annulat. Oefversigt af. kongl. Vetenskaps Akadamiens Förhandlmgar, 1867.

**King, H. D.**
'98. Regeneration in Asterias vulgaris Arch. f. Entw.-mech., VII, 1898.
'00. Further Studies on Regeneration in Asterias vulgaris. *Ibid.*, IX, 1900.

**Klein, Edm. J.**
'95-'97. Regeneration, Transplantation und Autotomie im Thierreich. Fauna Luxemburg, 5-7, 1895-97.

**Knight, T. A.**
'09. On the Origin and Formation of Roots. Phil. Trans., 1809.

**Kny, L.**
'89. Umkehrversuch mit Ampelopsis quinquefolia. Berichte d. deutsch. botan. Gesellsch., VII, 1889.

**Kochs, W.**
'97. Versuche über Regeneration von Organen bei Amphibien. Arch. f. mikr. Anat., XLIX, 1897.

**Korschelt, E.**
'97. Über das Regenerationsvermögen der Regenwürmer. Sitzungsber. Ges. Naturw., Marburg, 1897.
'98. Über Regenerations- und Transplantationsversuche bei Lumbriciden. Ber. Zool. Ges., 1898.

**Kowalevski, A. F.**
'72. Über die Vermehrung der Seesterne durch Theilung und Knospung. Zeit. wiss. Zool., XXII, 1872.

**Krämer, A.**
'47. Über den Palolowurm, 1847.
'99. Palolo untersuchungen. Biol. Centralbl., XIX, 1899.
'99. Palolo untersuchungen in October und November, 1898. *Ibid.*

**Krauss, H.**
  '98. Selbstverstümmelungen bei den Heuschrecken. Prometheus, IX, 1898.

**Kroeber, J.**
  '00. An Experimental Demonstration of the Regeneration of the Pharynx of Allolobophora from Endoderm. Biol. Bulletin, II, 1900.

**Lacépède, B. G. E. de.**
  1788. Histoire naturelle des quadr. ovip. et des serpentes. 1788.

**Lang, A.**
  '88. Über den Einfluss der festsitzenden Lebensweise auf die Thiere. Jena, 1888.

**Lefèvre, G.**
  '98. Regeneration in Cordylophora. Johns Hopkins University Circulars, Feb. 8, 1898.

**Lessona, M.**
  '69. Sulla reproduzione della parte in multi animali. Atti della Soc. Ital., X, 1869.

**Lillie, F. R.**
  '96. On the Smallest Parts of Stentor capable of Regeneration. Journ. Morph., XII, 1896.

**Lillie, F. R., and Knowlton, F. P.**
  '97. On the Effect of Temperature on the Development of Animals. Zool. Bulletin, I, 1897.

**Lindemuth, H.**
  Über Bildung von Bulben, etc. Ber. bot. Gesell., XIV.

**Loeb, J.**
  '91. Untersuchungen zur physiologischen Morphologie der Tiere. I. Über Heteromorphose. Würzburg, 1891.
  '92. Untersuch., etc. II. Organbildung und Wachstum. Würzburg, 1892.
  '92. Investigations in Physiological Morphology. III. Experiments on Cleavage. Journ. Morph., VII, 1892.
  '94. On Some Facts and Principles of Physiological Morphology. Biol. Lect., Woods Holl, in 1893, 1894.
  '94. Über eine einfache Methode, zwei oder mehr zusammengewachsene Embryonen aus einem Ei hervorzubringen. Pflüger's Arch., LV, 1894.
  '94. Über die Grenzen der Teilbarkeit der Eisubstanz. Pflüger's Arch., LIX, 1894.
  '95. Beiträge zur Entwickelungmechanik der aus einem Ei entstehenden Doppelbildungen. Arch. f. Entw.-mech., I, 1895.
  '95. Bemerkungen über Regeneration. Arch. f. Entw.-mech., II, 1895.
  '96. Über den Einfluss des Lichts auf Organbildung bei Tieren. Pflüger's Arch., LXIII, 1896.
  '96. Hat das Centralnervensystem einen Einfluss auf die Vorgänge der Larvenmetamorphose? Arch. f. Entw.-mech., IV, 1896.
  '97. Zur Theorie der physiologischen Licht- und Schwerkraftwirkungen. Pflüger's Arch., LXVI, 1897.
  '98. On Egg-Structure and the Heredity of Instincts. Monist., VIII, 1898.
  '98. Assimilation and Heredity. Monist., VIII, 1898.
  '99. Über die angebliche gegenseitige Beeinflussung der Furchungzellen und die Entstehung der Blastula. Arch. f. Entw.-mech., VIII, 1899.
  '99. Warum ist die Regeneration kernloser Protoplasmastücke unmöglich oder erschwert? Arch. f. Entw.-mech., VIII, 1899.
  '00. On the Transformation and Regeneration of Organs. Am. Journ. of Physiol., IV, 1900.

**Loeb, L.**
  '97. Über Transplantation von Weisser Haut auf einen Defect in Schwarzer Haut und umgekehrt am Ohr des Meerschweinchens. Arch. f. Entw.-mech., VI, 1897.
  '98. Über Regeneration des Epithels. Arch. f. Entw.-mech., VI, 1898.
  '99. An Experiment-Study of Transformation of Epithelium to Connective Tissue. Medicin, 1899.

**McIntosh, W. C.**

'70. Notes on the Development of Lost Parts in the Nemerteans. Journ. Linn. Soc., X, 1870.

'73-'74. Marine British Annelids. 1873-74.

**Magnus, Albertus.**

1661. Ordinis praedicatorum de animalibus, Lib. XXVI, tome VI. Lugundi, MDCLI.

**Mall, F. P.**

'96. Reversal of the Intestine. Johns Hopkins Hospital Reports, I, 1896.

**Marenzeller, F. von.**

'79. Die Aufzucht des Badeschwamms aus Theilstücken. Verh. Zool.-bot. Ges. Wien., XXXVIII, 1879.

**Martinotti, C.**

'90. Über Hyperplasie und Regeneration der drüsigen Elemente in Beziehung auf ihre Functionsfähigkeit. Centralbl. f. allg. Pathol., I, 1890.

**Martins, E. von.**

'66. Über ostasiatische Echinodermen. Archiv. f. Naturgesch., L, 1866.

'84. Über das Wiedererzeugungsvermögen bei Seesternen. Sitz. d. Gesell. naturf. Freunde zu Berlin, 1884.

**Mayer, C.**

'59. Reproductionsvermögen und Anatomie der Naiden. Ver. Nat. Vereins, Rheinlande XVI, 1859.

**Mazza, F.**

'90. Sulla ringenerazione della pinna caudale in alcuni Pesci. Atti Soc. Ligust. Sc. N., I, 1890.

**Michel, A.**

'98. Recherches zur la régénération chez les Annelides. Bull. Sc. France et Belg., XXXI, 1898.

**Mingazzini, P.**

'91. Sulla rigenerazione nei Tunicati. Boll. Soc. Napoli, V, 1891.

**Monti, R.**

'00. Studi Sperimentali sulla Regenerazione nei Rebdoceli marini. Rendiconti d. R. Inst. Lomb. Sc. e Lett., (Ser. II,) XXXIII, 1900.

'00. La ringenerazione nelle Planarie marine. Mem. R. Inst. Lomb. Sc. Lett. Cl. Sc. Mat. Nat., XIX, 1900.

**Morgan, T. H.**

'93. Experimental Studies on the Teleost Eggs. Anat. Anz., VIII, 1893.

'93. Experimental Studies on Echinoderm Eggs. *Ibid.*, IX, 1893.

'95. A Study of Metamerism. Q. J. Micr. Sc., XXXVII, 1895.

'95. The Formation of the Fish Embryo. Jour. Morph., X, 1895.

'95. Half Embryos and Whole Embryos from one of the first two Blastomeres of the Frog's Egg. Anat. Anz., X, 1895.

'95. A Study of a Variation in Cleavage. Arch. f. Entw.-mech., II, 1895.

'95. Studies of the " Partial " Larvae of Sphaerechinus. *Ibid.*, II, 1895.

'95. The Fertilization of non-nucleated Fragments of Echinoderm-Eggs. *Ibid.*, II, 1895.

'96. The Number of Cells in Larvae from Isolated Blastomeres of Amphioxus. *Ibid.*, III, 1896.

'97. Regeneration in Allolobophora foetida. *Ibid.*, V, 1897.

'97. The Development of the Frog's Egg. New York, 1897.

'98. Developmental Mechanics. Science, N. S., VII, 1898.

'98. Experimental Studies of the Regeneration of Planaria maculata. Arch. f. Entw.-mech., VIII, 1898.

'98. Regeneration and Liability to Injury. Zool. Bulletin, I, 1898.

'99. Regeneration of Tissue composed of Parts of Two Species. Biol. Bulletin, I, 1899.

'99. Regeneration in the Hydromedusa, Gonionemus vertens. The American Naturalist, XXXIII, 1899.

'99. A Confirmation of Spallanzani's Discovery of an Earthworm regenerating a Tail in place of a Head. Anat. Anz., XV, 1899.

'99. Further Experiments on the Regeneration of Tissue composed of Parts of Two Species. Biol. Bulletin, I, 1899.

'99. Some Problems of Regeneration. Biological Lectures, Woods Holl (1898), 1899.

'00. Further Experiments on the Regeneration of the Appendages of the Hermit-Crab. Anat. Anz., XVII, 1900.

'00. Regeneration: Old and New Interpretations. Biological Lectures, Woods Holl (1899), 1900.

'00. Regeneration in Bipalium. Arch. f. Entw.-mech., IX, 1900.

'00. Regeneration in Planarians. *Ibid.*, X, 1900.

'00. Regeneration in Teleosts. *Ibid.*, X, 1900.

'01. Regeneration in Tubularia. *Ibid.*, XI, 1901.

'01. The Problem of Development. The International Monthly, 1901.

'01. The Factors that determine Regeneration in Antennularia. Biol. Bulletin, II, 1901.

'01. Regeneration of Proportionate Structures in Stentor. Biol. Bulletin, II, 1901.

'01. Regeneration in Planaria lugubris. Arch. f. Entw.-mech., XII, 1901.

**Morgan, T. H., and Tsuda, Umé.**

'93. The Orientation of the Frog's Egg. Q. J. Micr. Sc., XXXV, 1893.

**Müller, E.**

'96. Über die Regeneration der Augenlinse nach Extirpation derselben bei Tritonen. Arch. f. mikr. Anat., XLVII, 1896.

**Müller, F.**

'80. Haeckel's Biogenetische Grundgesetz bei der Neubildung verlorener Glieder. Kosmos, VIII, 1880–81.

**Müller, E.**

'95. Über das Wiederwachsen (Regeneration) von Körperteilen. Jahresb. d. Ver. f. vaterl. Naturk. in Württemberg, LVI, 1895.

**Müller, H.**

'64. Über Regeneration der Wirbelsäule und des Rückenmarkes bei Tritonen und Eidechsen. Frankfurt a. M., 1864.

**Müller, O. F.**

1771. Von Würmern des süssen und salzigen Wassers. 1771.

**Nägeli, C. von.**

'84. Mechanisch-physiologische Theorie der Abstammungslehre. 1884.

**Newport, G.**

'44. On the Reproduction of Lost Parts in Myriapoda and Insecta. Phil. Trans., 1844.

**Nussbaum, M.**

'84. Über spontane und künstliche Zellteilung. Sitz. d. Niederrh. Ges., 1884.

'86. Über die Teilbarkeit der lebendigen Materie. I. Die spontane und künstliche Teilung der Infusorien. Arch. f. mikr. Anat., XXVI, 1886.

'87. Über die Teilbarkeit, etc. II. Beiträge zur Naturgeschichte des Genus Hydra. Arch. f. mikr. Anat., XXIX, 1887.

'91. Mechanik des Trembleyschen Umstülpungsversuchs. Arch. f. mikr. Anat., XXXVI, 1891.

'94. Die mit der Entwickelung fortschreitende Differenzierung der Zellen. Sitz.-Ber. Niederrh. Ges. Bonn, 1894.

**Nussbaum, J., and Sidoriak, S.**

'90. Beiträge zur Kenntnis der Regenerationsvorgänge nach Künstlichen Verletzungen bei älteren Bachforellen embryonen (Salmo fario. L.). Arch. f. Entw.-mech., X, 1890.

**Parke, H. H.**

'00. Variation and Regulation of Abnormalities in Hydra. Arch. f. Entw.-mech., X, 1900.

**Parker, G. H., and Burnett, F. L.**

'00. The Reactions of Planarians with and without Eyes to Light. Am. Journ. Physiol., IV, 1900.

**Parona, C.**

'91. L'Autotomie e la regeneratione delle appendici dorsale nella Tethys lepornia. Atti della R. Universita di Genova, VII, 1891. (Also Zool. Anz., XIV, 1891.)

**Peebles, Florence.**

'97. Experimental Studies on Hydra. Arch. f. Entw.-mech., V, 1897.

'98. The Effect of Temperature on the Regeneration of Hydra. Zool. Bull., II, 1898.

'oo. Experiments in Regeneration and in Grafting of Hydrozoa. Arch. f. Entw.-mech., X, 1900.

**Perrier, Ed.**

'72. Recherches sur l'Anatomie et la Régénération des Bras de la Comatula rosacea. Arch. Zool. Expérim., II, 1872.

'73. Sur l'Autotomie et la Régénération des Bras de la Comatula. Arch. Zool. Expérim., II, 1873.

**Peters, A.**

'89. Uber die Regeneration des Endothels der Cornea. Arch. f. Mikr. Anat., XXXIII, 1889.

**Petrone, A.**

'84. Du processes régénérateur sur le poumon, sur la foie et sur le rein. Archiv. Ital. d. Biol., V, 1884.

**Pfeffer, W.**

'97. Pflanzenphysiologie, 1897.

**Pflüger, E.**

'77. Die teleologische Mechanik der lebendigen Natur. Pflüger's Arch., XV, 1877.

'83. Über der Einfluss der Schwerkraft auf die Teilung der Zellen. Pflüger's Arch., XXXI, 1883.

'83. Über den Einfluss der Schwerkraft auf die Teilung der Zellen und auf die Entwickelung des Embryos. Pflüger's Arch., XXXII, 1883.

'84. Über die Einwirkung der Schwerkraft und anderer Bedingungen auf die Richtung der Zellteilung. Pflüger's Arch., XXXIV, 1884.

**Phillipeaux, J. M.**

'66–'67. Experience démontrant que les membres de la salamandre aquatique (Triton cristatus) ne se régénèrent, etc. Compt. Rend. d. l'Acad. de Science, 1866–67.

'67. Sur la régénération des membres chez l'Axolotl (Siren pisciformis). *Ibid.*, 1867.

'74. Note sur les résultats de l'extirpation complète d'un des membres antérieurs sur l'Axolotl et sur la salamandre aquatique. Gaz. Méd. de Paris, 1874.

'76. Expériences montrant que les mamelons extirpés sur des jeunes Cochons d'Inde ne se régénèrent point. Compt. Rend., 8 Fev., 1876.

'76. Les membres de la salamandre aquatique bien extirpés ne se régénèrent point. Compt. Rend., LXXXII, Nr. 20, 1876.

'79. Note sur la régénération de l'humeure vitrée chez les animaux vivant, lapins, cochons d'Inde. Gaz. Méd. de Paris, 1879.

'79. Sur le rétablissement de la vue chez les cochons d'Inde après l'extraction des humeurs vitrée et cristalline. Gaz. Méd. de Paris, 1879.

'80. Note sur la production de l'oeil chez la salamandre aquatique. Gaz. Méd. de Paris, 1880.

**Piana, G.**

'94. Ricerche sulla polidactilia acquisita determinata sperimentale nei tritoni e sulla coda supernumera nelle lucertole. Ric. Lab. di Anat. norm. di Roma, IV, 1894.

**Pliny, Secundus.**

77. Secundi historia mundi. Lib. XXXVII, Lib. XI.

**Ponfick, E.**

'90. Über Rekreation der Leber. Verhandl. des X Intern. Kongresses zu Berlin, II, 1890.

**Porta, Jo. Baptista.**

1650. Neapolitani magiae naturalis libri viginti. Rhotomagi MDCL. Lib. II.

x

**Prantl, K.**
'74. Untersuch. über die Regeneration des Vegetations-punktes an Angiospermenwurzeln. Arb. a. d. Bot. Instit. in Würzburg, IV, 1874.

**Preyer, W.**
'86. Über die Bewegungen der Seesterne. Mitth. Zool. Stat. Neapol., VII, 1886–87.

**Pringsheim, G.**
'76. Über Vegetative Sprossen der Moosfrüchte. Monatsberichte d. k. Akad. d. Wiss. zu Berlin, Juli, 1876.

**Przibram, H.**
'96. Regeneration bei den Crustaceen. Zool. Anz., XIX, 1896.
'99. Die Regeneration bei den Crustaceen. Arb. d. Zool. Inst. in Wien., II, 1899.
'00. Experimentelle Studien über Regeneration. Biol. Centralbl., XX, 1900.

**Quatrefages, A.**
'65. Histoire naturelle des Annélées. I (page 126), 1865.

**Rand, H. W.**
'99. Regeneration and Regulation in Hydra viridis. Arch. f. Entw.-mech., VIII, 1899.
'99. The Regulation of Graft-Abnormalities in Hydra. Arch. Entw.-mech. IX, 1899.

**Randolph, Harriet.**
'92. The Regeneration of the Tail in Lumbriculus. Jour. Morph., VII, 1892.
'97. Observations and Experiments on Regeneration in Planarians. Arch. f. Entw.-mech., 5, 1897.

**Rankin, D. R.**
'57. On the Structure and Habits of the Slowworm (Anguis fragilis Linn.). Edinburgh New Philos. Jour. (N. S.), V, 1857.

**Rauber, A.**
'95. Die Regeneration der Krystalle, I. Leipzig, 1895. II, 1896.

**Réaumur, R. A. de.**
1712. Sur les diversées Reproductions. Mem. d. l'Acad., 1712.
1742. Mémoires pour servir à l'histoire des Insectes. Tome VI, Préface, 1742.

**Ribbert, H.**
'94. Beiträge zur kompensatorischen Hypertrophie und zur Regeneration. Arch. f. Entw.-mech. I, 1894.
'97. Über Veränderungen transplantierter Gewebe. Arch. f. Entw.-mech. VI, 1897.
'97. Über Rückbildung an Zellen und Geweben und über die Entstehung der Geschwülste. Bibl. med. Abt., C, 1897.
'98. Über Veränderungen der abnorm. gekrümmten Schwanzwirbelsäule des Kaninchens. Arch. f. Entw.-mech., VI, 1898.
'98. Über Transplantation von Ovarium, Hoden, und Mamma. Arch. f. Entw.-mech., VII, 1898.

**Rievel, H.**
'96. Die Regeneration des Vorderdarms und Enddarms bei einigen Anneliden. Zeit. wiss. Zool., LXII, 1896.

**Ritter, W. E., and Congdon, E. M.**
'00. On the Inhibition by Artificial Section of the Normal Fission Plane in Stenostoma. Proc. California Acad. Science, II, 1900.

**Röthig, P.**
'98. Über Linsenregeneration. Inaug.-Diss. Berlin, 1898.

**Roux, W.**
'83. Über die Bedeutung der Kernteilungsfiguren. Leipzig, 1883.
'85. Beiträge zur Entwickelungsmechanik des Embryo. I. Zur Orientierung über einige Probleme der embryonalen Entwickelung. Zeit. f. Biologie, XXI, 1885.
'84. II. Über die Entwickelung des Froscheies bei Aufhebung der richtenden Wirkung der Schwere. Breslauer aerztl. zeitsch., 1884.
'85. III. Über die Bestimmung der Hauptrichtungen des Froschembryo im Ei und über die erste Teilung des Froscheies. *Ibid.*, 1885.

'87. IV. Die Bestimmung der Medianebene des Froschembryo durch die Kopulations-richtung des Eikernes und des Spermakernes. Arch. f. mikr. Anat., XXIX, 1887.

'88. V. Über die künstliche Hervorbringung halber Embryonen durch Zerstörung einer der beiden ersten Furchungskugeln, etc. Virchow's Archiv, CXIV, 1888.

'91. VI. Über die morphologische Polarization von Eiern und Embryonen durch den elektrischen Strom. Sitz. Ber. Akad. Wiss. Wien., CI, 1891.

'90. Die Entwickelungsmechanik der Organismen, eine anatomische Wissenschaft der Zukunft. Wien, 1890.

'92. Über das entwickelungsmechanische Vermögen jeder der beiden ersten Furchungs-zellen des Eies. Verhandl. Anat. Gesell. Wien., 1892.

'93. Über Mosaikarbeit und neuere Entwickelungshypothesen. Anat. Hefte, II, 1893.

'93. Über die Spezifikation der Furchungszellen und über die bei der Postgeneration und Regeneration anzunehmenden Vorgänge. Biol. Centralbl., XIII, 1893.

'94. Über den Cytotropismus der Furchungszellen des Grasfrosches. Arch. f. Entw.-mech., I, 1894.

'95. Gesammelte Abhandlungen über Entwickelungsmechanik. Leipzig, 1895.

'95. Über die verschiedene Entwickelung isolierter erster Blastomeren. Arch. f. Entw.-mech., I, 1895.

'96. Über die Selbstordnung (Cytotaxis) sich berührender Furchungszellen, etc. *Ibid.*, III, 1896.

'96. Über die Bedeutung "geringer" verschiedenheiten der relativen Grösse der Furchungszellen für den Charakter des Furchungsschemas. *Ibid.*, IV, 1896.

'97. Für unser Programm und seine Verwirklichung. *Ibid.*, V, 1897.

'96. Zu H. Driesch's "Analytischer Theorie der organischen Entwickelung." *Ibid.*, IV, 1896.

'00. Berichtigungen zu O. Schultze's jüngstem Aufsatz über die Bedeutung der Schwerkraft, etc. *Ibid.*, X, 1900.

**Sachs, J.**

'80. Stoff und Form der Pflanzenorgane. Arbeiten d. bot. Instituts Würzburg, II, 1880–82.

'93. Physiologische Notizen, I. Flora, 1893.

**Sarasin, P. and F.**

'88. Knospenbildung bei Linckia multiformis. Ergebn. Naturforschung auf Ceylon, 1884–85. I. Wiesbaden, 1888.

**Sars, G. O.**

'75. Researches on the Structure and Affinity of the Genus Brisinga. Christiania, 1875.

**Schaper, A.**

'98. Experimentelle Studien an Amphibienlarven. I. Haben künstlich angelegte De-fekte des Centralnervensystems oder die vollständige Elimination desselben einen nachweisbaren Einfluss auf die Entwickelung des Gesamtorganismus junger Frosch-larven? Arch. f. Entw.-mech., VI, 1898.

**Schiedt, R. R.**

'92. Diffuse Pigmentation of the Epidermis of the Oyster due to prolonged exposure to Light. Regeneration of Shell and loss of Adductor Muscle. Proc. Acad. Nat. Sci. Phila., 1892.

**Schimkewitsch, W.**

'00. Über einer Fall von Heterotopie der Haare. Verh. d. k. Naturforscher Gesell. in St. Petersburg, XXX, 1900.

**Schmidt, E. O.**

'75. Spongien. Jahresb. Comm. Untersuch. Deutschen Meere in Kiel, II und III, Jahrg., 1875.

**Schostakowitsch.**

'94. Über Regeneration, etc., bei Lebermoosen. Flora, Ergänzungsband, 1894.

**Schultz, E.**

'98. Über die Regeneration von Spinnenfüssen. Trav. Soc. Nat. Petersb., XXIX, 1898.

**Schultze, E.**
'99. Aus dem Gebiete der Regeneration. Zeit. f. wiss. Zool., LXVI, 1899.

**Schultze, L. S.**
'99. Die Regeneration des Ganglion von Ciona intestinalis, L. und über das Verhaltnis der Regeneration und Knospung zur Keimblätterlehre. Jena Zeit. f. Naturwiss., XXXIII, 1899.

**Schultze, O.**
'94. Die künstliche Erzeugung von Doppelbildungen bei Froschlarven mit Hülfe abnormer Gravitationswirkung. Arch. f. Entw.-mech., I, 1894.
'99. Über das erste Auftreten der bilateralen Symmetrie im Verlauf der Entwickelung. Archiv. f. Mikr. Anat., LV, 1899.
'99. Über die Nothwendigkeit der freien Entwickelung des Embryo. *Ibid.*, 1899.

**Scudder, S.**
'68-'69. Proceedings Boston Society of Natural History (page 99), XII, 1868–69.

**Semon, R.**
'89. Neubildung der Scherbe in der Mitte eines abgebrochenen Seesternarmes. Jena. Zeit. f. Naturw., XXIII, 1889.

**Semper, C.**
'68. Reisen in Archipel der Philippinen, II, 1868.
'76. Die Verwandtschaftsbeziehungen der gegliederten Thiere. Arb. zool.-zoot. Inst. Würzburg, III, 1876.

**Siebold.**
'28. Observationes quaedam de Salamandris et Tritonis. Diss. Berolini, 1828.

**Simroth, H.**
'77. Anatomie und Schizogonie der Ophiactis virens. Zeit. f. wiss. Zool., XXVIII, 1877.

**Spallanzani, L.**
1782. Risultati di esperienze sopra la riproduzione della Testa nelle Lumache Terrestri. Memoria di Matematica e Fisica della Societa italiana, tomo I, Verona, 1782.
'26. Prodromo di un' opera sopra le riproduzioni animali. Milano, 1826.

**Spemann, H.**
'00. Experimentelle Erzeugung zweiköpfiger Embryonen. Sitzber. d. Phys. Med. Gesell. Würzburg, 1900.
'01. Entwickelungsphysiologische Studien am Triton-Ei. Archiv. f. Entw.-mech., XII, 1901.

**Spengel, J. W.**
'93. Monographie der Enteropneusten. Fauna und Flora des Golfes von Neapel, 1893.

**Stahl, E.**
'76. Über künstliche hervorgerufene Protonemabildungen an dem Sporogonium der Laubmoose. Bot. Zeit., 1876.

**Strasser, H.**
'99. Regeneration und Entwickelung. Berner Rektoratsrede. Jena, 1899.

**Studer, Th.**
'77. Echinodermen aus dem antarktischen Meere. Monatsber. d. Berliner Akad., 1877.

**Tittmann, H.**
'95. Physiol. Untersuch. über Callusbildung an Stocklingen. Jahr. f. wiss. Botan., XXVIII, 1895.

**Tizzoni, G.**
'83. Experimentelle Studie über die partielle Regeneration und Neubildung von Lebergewebe. Biol. Centralb., III, 1883–84.

**Tornier, G.**
'96. Über Hyperdaktylie, Regeneration und Vererbung mit Experimenten. Arch. f. Entw.-mech., III, 1896.
'97. Über experimentell erzeugte dreischwänzige Eidechsen und Doppelgliedmassen von Molchen. Zool. Anz., XX, 1897.

'97.  Über Operationsmethoden, welche sicher Hyperdaktylie erzeugen mit Bemerkungen über Hyperdaktylie und Hyperpedie.  Zool. Anz., XX, 1897.

**Tower, W. L.**
'99.  Loss of the Ectoderm of Hydra viridis in the Light of a Projection Microscope. The American Naturalist (page 505), June, 1899.

**Towle, E. W.**
'91.  On Muscle Regeneration in the Limbs of Plethedon.  Biol. Bull., II, 1891.

**Trembley, A.**
'74.  Mémoires pour servir à l'histoire d'un genre de Polypes d'eau douce.  Leide, 1774.

**Tytler, R. C.**
'65.  Farbenwechsel, die Häutung und die Regeneration des Schwanzes bei den Ascalaboten.  Journ. of the Asiatic Soc. of Bengal, 1865.

**Vernon, H. M.**
'99.  The Effect of Staleness of the Sexual Cells on the Development of Echinoids. Proc. Roy. Soc., LXV, 1899.
'00.  Cross-Fertilization among Echinoids.  Arch. f. Entw.-mech., IX, 1900.

**Verworn, M.**
'91.  Die physiologische Bedeutung d. Zellkerns.  Arch. f. d. ges. Physiol., LI, 1891.
'88.  Biologische Protistenstudien.  I.  Zeit. f. wiss. Zool., XLVI, 1888.
'89.  Psycho-physiologische Protistenstudien, 1889.
'89.  Die Polare Erregung der Protisten durch den galvanischen Strom.  Arch. f. d. ges. Physiol., XLVI, 1889.

**Vöchting, H.**
'77.  Über die Teilbarkeit und die Wirkung innerer und äusserer Kräfte auf die Organbildung in Pflanzenteilen.  Pflüger's Arch., XV, 1877.
'78.  Über Organbildung im Pflanzenreiche.  Bonn, 1878 u. 1884.
'85.  Über die Regeneration der Marchantieen.  Jahrb. f. wiss. Botanik, XVI, 1885.
'87.  Über die Bildung von Knollen.  Bibliotheca Botanica, No. 4, Cassel, 1887.
'92.  Über Transplantation am Pflanzenkörper.  Tübingen, 1892.

**Voigt, W.**
'99.  Künstlich hervorgerufene Neubildung von körpertheilen bei Strudelwürmern, Sitz. d. Niederrhein. Gesell. f. Natur- und Heilkunde zu Bonn, 1899.

**De Vries, H.**
'89.  Intracellulare Pangenesis, 1889.

**Vulpian, M. A.**
'59.  Notes sur les phénomènes de développement qui se manifestent dans la queue de très jeunes embryons de grenouille.  Compt. Rend., XLVIII, 1859.

**Wagner, F. von.**
'93.  Einige Bemerkungen über das Verhältnis von Ontogenie und Regeneration.  Biol. Centralbl., XIII, 1893.
'97.  Zwei Wörter zur Kenntniss der Regeneration des Vorderdarms bei Lumbriculus. Zool. Anz., XX, 1897.
'00.  Beiträge zur Kenntniss der Reparationsprozesse bei Lumbriculus variegatus.  I. Zool. Jahrb., XIII, 1900.

**Wagner, W.**
'87.  La régénération des organes perdus chez les araignées.  Bull. Soc. Imp. Natural., Moscow, 1887.

**Watson, J.**
'91.  On the Redevelopment of Lost Limbs in the Insecta.  The Entomologist, XXIV, 1891.

**Weismann, A.**
'91.  Essays on Heredity, Vol. I.  Clarendon Press, Oxford, 1891.
'92.  Das Keimplasma.  Eine Theorie der Vererbung.  Jena, 1892.
'94.  The Germ-plasm.  New York, 1894.
'96.  Über Germinal-Selektion.  Eine Quelle bestimmt gerichteter Variation.  Jena, 1896.

'97.   Regeneration : Facts and Interpretations.   Natural Science, April, 1897.

'99.   Thatsachen und Auslegungen in Besug auf Regeneration.   Anat. Anz., XV, 1899.

**Wendelstadt, H.**

'01.   Über Knochenregeneration.   Arch. f. mikr. Anat., LVII, 1801.

**Werner, F.**

'92.   Selbstverstümmelung bei Heuschrecken Zool. Anz., XV, 1892.

'96.   Über die Schuppenbildung des regenerierten Schwanzes bei Eidechsen.   Sitzungsber. d. kais. Akad. in Wien, CV, 1896.

**Wetzel, G.**

'95.   Transplantationsversuche mit Hydra.   Arch. f. mikr. Anat., XLV, 1895.

'95.   Über die Bedeutung der cirkulären Furche in der Entwickelung der Schultzeschen Doppelbildungen von Rana Fusca.   Arch. f. mikr. Anat., XLVI, 1895.

'96.   Beitrag zum Studium der künstlichen Doppelmissbildungen von Rana Fusca. Inaug. Dissert., 1896.

**Whitman, C. O.**

'89.   The Seat of Formative and Regenerative Energy.   Jour. Morph., II, 1889.

'93.   The Inadequacy of the Cell Theory of Development.   Jour. Morph., VIII, 1893.

'95.   Evolution and Epigenesis.   Biolog. Lectures at Woods Holl in 1894, 1895.

**Wiedersheim, R.**

'77.   Über Neubildung von Kiemen bei Siren lacertina.   Morph. Jahrb., III, 1887.

**Wilson, C. B.**

'97.   Experiments on the Early Development of the Amphibian Embryo under the Influence of Ringer and Salt Solutions.   Arch. f. Entw.-mech., V, 1897.

'00.   The Habits and Early Development of Cerebratulus Lacteus.   Q. J. Mic. Sc., XLIII, 1900.

**Wilson, E. B.**

'92.   The Cell-Lineage of Nereis.   Jour. Morph., VI, 1892.

'93.   Amphioxus and the Mosaic Theory of Development.   Jour. Morph., VIII, 1893.

'95.   On Cleavage and Mosaic Work.   Appendix to Crampton.   Arch. f. Entw.-mech., III, 1895.

'96.   The Cell in Development and Inheritance.   New York and London, 1896.

'98.   Considerations on Cell-Lineage and Ancestral Reminiscence.   New York Acad. Science, II, 1898.

**Wolff, G.**

'94.   Bemerkungen zum Darwinismus mit einem experimentellen Beitrag zur Physiologie der Entwickelung.   Biol. Centralbl., XIV, 1894.

'93.   Entwickelungphysiologische.   Studien.   I.   Die Regeneration der Urodelenlinse. Arch. f. Entw.-mech., I, 1893.

**Zacharias, O.**

'86.   Über Fortpflanzung durch Spontanquertheilung, etc.   Zeit. f. wiss. Zool., XLIII, 1886.

**Ziegler, E.**

'91.   Über die ursachen der pathologischen Gewebsneubildungen.   International Beiträge zur wissenschaftliche Medizin.   Festschrift für Virchow, II, 1891.

**Ziegler, H. E.**

'98.   Experimentelle Studien über die Zellteilung, I.   Die Zerschnürung der Seeigeleier. Arch. f. Entw.-mech., VI, 1898.

'98.   Experimentelle Studien, etc., III.   Die Furchungszellen von Beroë ovata.   Arch. f. Entw.-mech., VII, 1898.

**Zoja, R.**

'95.   Sullo sviluppo dei blastomeri isolati delle uova di alcune meduse.   Arch. f. Entw.-mech., I u. II, 1895.

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